



THE UNIVERSITY *of* EDINBURGH

This thesis has been submitted in fulfilment of the requirements for a postgraduate degree (e.g. PhD, MPhil, DClinPsychol) at the University of Edinburgh. Please note the following terms and conditions of use:

- This work is protected by copyright and other intellectual property rights, which are retained by the thesis author, unless otherwise stated.
- A copy can be downloaded for personal non-commercial research or study, without prior permission or charge.
- This thesis cannot be reproduced or quoted extensively from without first obtaining permission in writing from the author.
- The content must not be changed in any way or sold commercially in any format or medium without the formal permission of the author.
- When referring to this work, full bibliographic details including the author, title, awarding institution and date of the thesis must be given.

**Investigating the specificity of neuropsychological
performance in bulimic outpatients: a comparison
with anxious and depressed outpatients.**

Kate O'Sullivan

Doctorate in Clinical Psychology

University of Edinburgh

August 2012

D. Clin. Psychol. Declaration of own work

This sheet must be filled in (each box ticked to show that the condition has been met), signed and dated, and included with all assessments - work will not be marked unless this is done

Name: **Kate O'Sullivan**

Assessed work: Case Study Conceptualisation Research proposal Case Study
 SSR Essay Question Paper Thesis

Title of work: Investigating the specificity of neuropsychological performance in bulimic outpatients: a comparison with anxious and depressed outpatients.

I confirm that all this work is my own except where indicated, and that I have:

- Read and understood the Plagiarism Rules and Regulations ☐
- Composed and undertaken the work myself ☐
- Clearly referenced/listed all sources as appropriate ☐
- Referenced and put in inverted commas any quoted text of more than three words (from books, web, etc) ☐
- Given the sources of all pictures, data etc. that are not my own ☐
- Not made undue use of essay(s) of any other student(s) either past or present (or where used, this has been referenced appropriately) ☐
- Not sought or used the help of any external professional agencies for the work (or where used, this has been referenced appropriately) ☐
- Not submitted the work for any other degree or professional qualification except as specified ☐
- Acknowledged in appropriate places any help that I have received from others (e.g. fellow students, technicians, statisticians, external sources) ☐
- Complied with other plagiarism criteria specified in the Programme Handbook ☐
- I understand that any false claim for this work will be penalised in accordance with the University regulations ☐

Signature **Date**

Please note:

a) If you need further guidance on plagiarism, you can:

i/ Speak to your director of studies or supervisor

ii/ View university regulations at <http://www.ed.ac.uk/schools-departments/academic-services/policies-regulations>

Acknowledgements

The completion of this thesis required time and assistance from a number of people. I am very grateful to all of the participants who gave up their time to contribute to this study and to all of the clinicians who looked for participants among their caseload. I would particularly like to thank Seonaid Cleare, Yvonne Peebles, Dr Suzanne Deas, Jan Templeton, Dr Kenny Day, Dr Kirsty McLean and Dr Paula Collin who acted as key contacts within their departments and helped to maintain clinicians' awareness of the study when I was unable to be present. I would also like to thank my colleague Moira Cook for sharing her knowledge of neuropsychological testing.

My clinical supervisors Professor Kevin Power, Dr Paula Collin and Dr Alison Livingstone have been a great help throughout the study. I would like to thank my academic supervisor, Dr Emily Newman, for her time and support. Her input into the revision of chapters was invaluable and she was always available for advice and discussion.

My excellent friends and family have been an invaluable resource and support. Thank you all for reading drafts of chapters and helping me to stay calm and focused.

Contents

Chapter 1: Introduction	13
1.2 Introduction to Thesis	13
1.3 Overview of Chapters	13
1.3.1 Chapter 2 – Systematic Review	13
1.3.2 Chapter 3 – Bridging Chapter	14
1.3.3 Chapter 4 – Journal Article	14
1.3.4 Chapter 5 – Methods	14
1.3.5 Chapter 6 – Additional Results	14
1.3.6 Chapter 7 – Additional Discussion	15
Chapter 2: Systematic Review	16
2.1 Introduction	17
2.2 Methods.....	19
2.2.1 Search Strategy.....	19
2.2.2 Inclusion and exclusion criteria	19
2.2.3 Data Extraction.....	21
2.2.4 Assessment of methodological quality.....	22
2.3 Results	26
2.3.1 Search results and characteristics of studies	26
2.3.2 Findings of the review.....	26
2.3.3 Memory	26
2.3.4 Attention, perception and working memory	31
2.3.5 Visuospatial Ability	32
2.3.6 Executive function	35
2.3.7 Summary of Neuropsychological findings.....	37
2.3.8 Assessment of Methodological Quality	37

2.4	Discussion	39
2.4.1	Limitations	41
2.4.2	Recommendation/implication for future research.....	42
2.4.3	Conclusion	42
2.5	References	43
Chapter 3:	Bridging Chapter	49
3.1	The Cognitive Model of Bulimia Nervosa.....	49
3.1.1	The Self liking/ Self Competence scale (Tafarodi & Swann, 2001)....	50
3.1.2	Social Problem Solving Inventory (SPSI) (D’Zurilla <i>et al.</i> , 2002).....	50
3.1.3	Impulsivity	52
3.2	Composition of the Patient groups used in this study	52
3.2.1	Gender of Participants.....	53
3.3	Research Links of the current study	54
3.4	Summary	54
3.4.1	Study Aims.....	55
Chapter 4:	Investigating the specificity of neuropsychological impairment in bulimic outpatients: a comparison with anxious and depressed outpatients.....	56
4.1	Introduction	56
4.2	Methods.....	61
4.2.1	Participants.....	61
4.2.2	Measures	65
4.2.3	Measures selected as a priori key variables for set shifting and inhibition	68
4.2.4	Procedure/Protocol.....	69
4.2.5	Data Analysis	69
4.3	Results	70

4.3.1	Group comparisons on psychological and neuropsychological measures	70
4.3.2	Relationship of Psychopathological Symptoms to Set Shifting and inhibition	73
4.3.3	Post hoc exploratory analysis.....	75
4.3.4	Exploratory analysis of performance on secondary set shifting and inhibition variables.....	77
4.4	Discussion	78
4.4.1	Limitations	80
4.4.2	Implications and future directions.....	81
4.4.3	Conclusion	81
4.5	References	82
Chapter 5:	Methodology	87
5.1	Design	87
5.2	Participants.....	87
5.2.1	Inclusion/exclusion criteria	87
5.2.2	The BN Group: Outpatients with Bulimia Nervosa or EDNOS-BN ...	90
5.2.3	The AD Group: Outpatients with Anxiety and/or Depression.....	91
5.3	Additional Descriptive data for BN and AD groups.....	92
5.4	Measures	93
5.4.1	Psychological Measures	93
5.4.2	Neuropsychological Measures	99
5.5	Procedure.....	104
5.5.1	The BN Group: Patients with Bulimia/EDNOS-BN.....	105
5.5.2	The AD Group: Patients being treated for anxiety or depressive disorders in the Adult Psychological Therapies Service.....	107
5.5.3	Recruitment activity at the level of clinicians.....	107

5.6	Ethical Issues.....	108
5.6.1	Approval.....	108
5.6.2	Confidentiality	108
5.6.3	Data Storage	109
5.6.4	Potential Distress to Participants/Disclosure of risk issues.....	110
5.7	Data analysis	111
5.7.1	Investigating assumptions for parametric statistical testing.....	111
5.7.2	Main analysis	111
5.7.3	Additional Analysis.....	112
5.7.4	Missing Data	113
5.8	Statistical Power and Sample Size	113
5.8.1	Difficulties identifying appropriate data for use in determining sample size	115
Chapter 6:	Additional Results.....	116
6.1	Further analysis of data presented in Chapter 4.....	116
6.1.1	Assessing Normality of the Data.....	116
6.1.2	Further details on analysis of Age normed scaled scores for a priori variables	118
6.1.3	Relationship of general and eating psychopathology	118
6.1.4	Clinically Significant Impairment.....	120
6.1.5	Relationships between performance on different neuropsychological measures.....	122
6.2	Non-key Executive function measures and additional subscales of the SCL-90-R	124
6.3	Analysis Relating to Aim 3 - Social Problem Solving and Self Esteem..	124
6.3.1	Social Problem Solving Style	124
6.3.2	Group comparisons of self esteem and social problem solving.....	125

6.3.3	Relationship between a priori variables and Social Problem Solving	128
6.3.4	Relationship between a priori variables and Self-Liking and Self-Competence.....	129
Chapter 7:	Additional Discussion	131
7.1	Age differences between groups	131
7.2	Relationships of general and eating pathology	131
7.3	Clinically significant impairment.....	131
7.4	Relationships between performance on neuropsychological measures ...	133
7.5	Non-key Executive Function Measures	134
7.6	Aim 3 – Social Problem Solving and Self Liking/Self Competence	134
7.7	Limitations	135
7.8	Implications and future directions.....	135
7.9	Conclusion	136
Chapter 8:	References	137
Appendices	154

Table of Tables

Table 2.1	Key Study Characteristics	23
Table 2.2	Quality Criteria applied to Reviewed studies	25
Table 2.3	Verbal memory in panic disorder compared to healthy controls	28
Table 2.4	Visual memory in panic disorder compared to healthy controls	30
Table 2.5	Working memory in panic disorder compared to healthy controls.....	34
Table 2.6	Executive function in panic disorder compared to healthy controls.....	36
Table 4.1	Diagnoses of AD group	62
Table 4.2:	Characteristics of groups.....	64
Table 4.3:	Comparison of groups on psychological variables	71

Table 4.4: Comparison of groups on key Set Shifting and inhibition variables	72
Table 4.5: Correlation of Set shifting and inhibition key measures with psychopathology measures in bulimic group	74
Table 4.6 Correlation of key set shifting and inhibition measures with psychopathology in the AD group	74
Table 4.7: Correlation of key set shifting and inhibition measures with psychopathology in both groups combined	75
Table 4.8: Adjusted Beta values for predictor variables in the regression analyses ..	77
Table 5.1: Demographic information for categorical data in Bulimic and Anxious/Depressed group	92
Table 5.2 Psychological Measures	93
Table 5.3 Subscales of the SPSI-R.....	98
Table 5.4 Neuropsychological Measures and Primary Areas Assessed	99
Table 6.1 Test of Normality Assumptions	117
Table 6.2 Correlation of general and eating psychopathology in BN group	119
Table 6.3 Correlation of general and eating psychopathology in AD group	120
Table 6.4: Number of participants demonstrating underperformance and impairment	121
Table 6.5 Relationship between performance on set shifting and inhibition measures in the BN group.....	122
Table 6.6 Relationship between performance on set shifting and inhibition measures in the anxious and/or depressed group	123
Table 6.7: Comparison of groups on additional psychological variables and non key executive function measures	127
Table 6.8: Correlation of Social Problem Solving Patterns and a priori variables in the BN group	128
Table 6.9 Correlation of Social Problem Solving Patterns and a priori variables in the AD group.....	129
Table 6.10: Association between a priori variables and self liking/self competence	130

Table of Figures

Figure 2.1 Flowchart showing search results, and the number of included and excluded studies.	21
Figure 5.1 Participant Journey	105
Figure 6.1 Social Problem Solving Styles of the BN group	125
Figure 6.2 Social Problem Solving Styles of the AD group	125

Table of Appendices

Appendix 1 Author Guidelines for Journal of Affective Disorders.....	155
Appendix 2 Systematic Review Database Search Terms	162
Appendix 3 Detailed Search Diagram for Systematic Review	170
Appendix 4 Details of Quality Criteria	172
Appendix 5 Author Guidelines for Journal of the International Neuropsychological Society.....	174
Appendix 6 Journal Article - Graphs relating to Correlations	178
Appendix 7 Invitation letter to NHS Grampian Participants	181
Appendix 8 Participant Information Sheets	182
Appendix 9 Letters of Ethical Approval	194
Appendix 10 Consent form	204
Appendix 11 Graphs of Correlations relating to Additional Results section.....	205

Thesis Abstract

Background

Eating Disorder research has highlighted the role of neuropsychological functioning, informing the treatment of Anorexia Nervosa. There is ambiguity in the data relating to cognitive impairment in Bulimia Nervosa, with the latest review providing inconclusive results. Executive function impairments in the area of set shifting and inhibition reported in BN are proposed to relate to traits of compulsivity and impulsivity. Other psychological disorders have also demonstrated executive function impairments. Among anxiety disorders, only PTSD and OCD have strong evidence of executive function deficits while a number of studies point towards executive function deficits in depression. This thesis aims to investigate the specificity of cognitive impairments seen in a group of female outpatients with bulimia nervosa, using a clinical comparison group of anxious and/or depressed female outpatients.

Methods

A systematic review was conducted to address a gap in the anxiety disorder literature and assess the neuropsychological profile of panic disorder. In order to address the main study aims, a comparison between a group of patients with BN and an anxious depressed group was conducted on neuropsychological measures of the Trail Making Test, Wisconsin Card Sorting Test, Hayling and Brixton tasks, Stroop and Verbal Fluency. In addition, psychological symptoms were assessed using SCL-90-R, Yale-Brown Obsessive Compulsive Scale and the Self-liking Self Competence scale. Social problems solving skills were assessed as a potential real world effect of executive function difficulties associated with eating disorders. The relationships between psychological and neuropsychological variables were investigated.

Results

The systematic review concluded that there was limited evidence of specific impairment in short term memory in panic disorder. The empirical study indicated no group differences on the above neuropsychological measures. Groups also did not differ on NART estimated IQ or self reported psychological symptoms. No

relationships were found between psychological symptoms and neuropsychological measures. Few individual participants were found to be impaired on neuropsychological measures in either group. However, those impaired in the BN group were exclusively impaired on the non-perseverative errors and categories completed variables of the WCST, which is thought to be related to impulsivity.

Conclusion

These findings suggest that the neuropsychological profile of bulimia is broadly similar to that of an anxious and/or depressed clinical group on measures of set shifting and inhibition. Although there was evidence of a deficit in inhibition among patients with bulimia further investigation is required.

Chapter 1: Introduction

1.2 Introduction to Thesis

This thesis focuses on the neuropsychological profile of Bulimia Nervosa (BN). Neuropsychological impairment in psychological disorders is a popular field of research as links between cognitive impairments central to a disorder and its symptoms can serve to identify predictors of the course of the illness (Keefe, 1995) and treatment outcomes (Porter *et al.*, 2007). Knowledge about the specific cognitive profile of a disorder can also contribute to the development of disorder specific cognitive models and therapies (Dudley *et al.*, 2011)

The aim of this thesis is to contribute to the body of research investigating the neuropsychological profile of BN by considering the specificity of the cognitive impairments reported in the literature. It is hoped that research into neuropsychological deficits in BN could increase our understanding of the disorder and inform treatment as it has in anorexia nervosa (AN) and schizophrenia (Kurtz *et al.*, 2001; Tchanturia *et al.*, 2008). The potentially confounding influences of comorbid anxiety disorders and depression in BN have been highlighted in recent reviews as a neglected area of research (Van den Eynde *et al.*, 2011; Zakzanis *et al.*, 2010). Therefore the current study incorporates a comparison group of anxious and/or depressed outpatients.

This chapter will provide an overview of the structure of this thesis submission.

1.3 Overview of Chapters

1.3.1 Chapter 2 – Systematic Review

Chapter 2 is a systematic review of the neuropsychological profile of panic disorder. This disorder has been selected, as a very recent review had comprehensively covered the neuropsychological profile of BN (Van den Eynde *et al.*, 2011). Common comorbidities of BN such as OCD (Martinez-Gonzalez & Piqueras-Rodriguez, 2008), PTSD (Polak *et al.*, 2012), social anxiety (O'Toole & Pedersen, 2011) and depression (Castaneda *et al.*, 2008) have also been recently reviewed. No specific review was available on GAD, specific phobia or panic disorder when the literature was examined, which are also frequently comorbid with BN. The panic

disorder review provided the opportunity to make a useful contribution to the literature and it allowed for a review of the appropriate size for thesis requirements.

1.3.2 Chapter 3 – Bridging Chapter

Chapter 3 provides a brief summary of the research and the aims of the thesis. It contains bridging information, which will introduce themes and literature that could not be included in the journal article introduction.

Information relating to Aims 1 and 2 are presented and discussed in the journal article (Chapter 4) and information relating to Aim 3 will be introduced in Chapter 3 and analysed and discussed as ‘additional’ data in Chapters 6 and 7.

1.3.3 Chapter 4 – Journal Article

Chapter 4 is a journal article reporting on the comparison between a group of females in psychological treatment for bulimia and a group of females in psychological treatment for anxiety and/or depression on neuropsychological measures of set shifting and inhibition.

This article explores whether the neuropsychological profile of BN involves patterns of performance that are specific to BN or shared by other psychiatric disorders. Similarly to BN, conflicting results have been published in the literature relating to possible neuropsychological deficits in people with anxiety disorders and depression, as described further in Chapter 4.

1.3.4 Chapter 5 – Methods

The journal article is followed by a comprehensive Methods Chapter including extended description of the measures used in the study and details relating to recruitment of participants.

1.3.5 Chapter 6 – Additional Results

The data presented in Chapter 4 are further analysed and data related to two additional neuropsychological measures (D-KEFS Verbal Fluency and the Brixton task) and two additional psychological measures (Self-liking/Self competence scale (SLSC) and the Social Problem Solving Inventory (SPSI)) are presented. Further introductory information related to the SLSC and SPSI is provided within the bridging information in Chapter 3.

1.3.6 Chapter 7 – Additional Discussion

Discussion related to all additional results is contained in this chapter.

Chapter 2: Systematic Review

(Written for the Journal of Affective Disorders, see author guidelines in Appendix 1. 7,319 words including tables)

Abstract

Background: There is a growing body of literature investigating the neuropsychological profile of Panic Disorder (PD), some of which suggests potential cognitive dysfunction. This paper systematically reviews the existing literature on neuropsychological performance in PD.

Method: PsychINFO, Embase, Medline and PsychArticles databases were searched to identify articles reporting on neuropsychological function in PD published in English during the time period 1980 to March 2012. 14 studies were identified.

Results: There was limited support for impairment in short term memory among individuals with PD, although this was not found across all studies. Overall, the reviewed studies did not support the presence of impairment in other areas of cognitive functioning, including executive function, long term memory, visuospatial or perceptual abilities and working memory.

Limitations: Studies containing samples of less than 15 participants per group were excluded from this review. A limited amount of research has been published on this topic and small sample sizes (under 25 per group) have been used by many studies. Therefore, the current review is based on a small number of studies with limited statistical power.

Conclusions: There is limited evidence of specific neuropsychological impairments in participants with PD. Impairments in short term memory have been noted in some of the literature, which warrants further investigation to establish its relevance to clinical practice. Larger sample sizes and appropriate statistical adjustment for multiple comparisons in future studies is highly recommended.

2.1 Introduction

Panic disorder (PD) is a disabling mental health problem characterised by unexpected, recurrent panic attacks, fear about the implications of attacks and modifications of behaviour as a result of the attacks (American Psychiatric Association, 2000). PD can occur with or without agoraphobia and is associated with high levels of psychiatric comorbidity and severe role impairment (Baillie & Rapee, 2005; Kessler et al., 2006).

A growing interest in the neurobiology of anxiety disorders in recent years has led to increasing research into neuropsychological deficits associated with them (Millan et al., 2012). Neuropsychological deficits are of interest, as they may be the basis for some key symptoms of PD and have implications for treatment, as has been seen in schizophrenia and anorexia (Cavedini et al., 2006; Tabarés-Seisdedos et al., 2008). The cognitive (Clark, 1986; Beck and Clark, 1997) and learning (Bouton et al., 2001) theoretical models of panic, support a role for biased information-processing of threat-related stimuli in the formation and maintenance of the disorder. This suggests that neuropsychological deficits in areas of information processing may underlie some symptoms of panic disorder. A large body of evidence suggests that patients with PD tend to selectively and automatically direct their attention towards threat-related stimuli (Ehlers et al., 1988; Clark et al., 1997; Lundh et al., 1999; Teachman et al., 2007). A difficulty shifting focus away from perceived threats could be related to difficulty with cognitive set shifting. Such difficulties have been reported in some neuropsychological studies of individuals with Panic Disorder (e.g. Airaksinen et al., 2005). Memory difficulties may also contribute to the biased appraisal of threat if examples of overcoming potentially threatening situations are not available in memory. Recent research suggests that memories of panic attacks may have the same qualities as traumatic memories, being poorly processed and involving re-experiencing which may keep them predominant in memory (Hagenaars et al., 2009). If underlying neuropsychological difficulties were found consistently in patients with PD, this would support the modification of common therapeutic interventions, such as CBT, or the incorporation of specific interventions to improve memory or set shifting ability, such as those that have been used successfully with individuals with anorexia (Tchanturia et al., 2008).

Neuropsychological deficits may also act as measurable symptoms of underlying neurobiological dysfunction. Several studies have found structural brain abnormalities in patients with anxiety disorders, including patients with PD (Mataix-Cols & van den Heuvel, 2006; Phan et al., 2009; Szeszko et al., 2005; van den Heuvel et al., 2005). Patterns of impairments in executive function have been reported in a number of recent reviews of neuropsychological performance in OCD (Martinez-Gonzalez & Piqueras-Rodriguez, 2008; Menzies et al., 2008; Olley et al., 2007). Executive function deficits have also been implicated in Post Traumatic Stress Disorder (PTSD). Anxiety disorders such as social anxiety disorder (SAD) and PD have been less well researched.

In PD, some imaging studies have indicated abnormalities in specific brain regions compared to controls, including different metabolic activity in the hippocampal and parahippocampal areas (Bisaga et al., 1998) and abnormalities in the temporal lobe structures (Vythilingam et al., 2000). However, Reiman and colleagues have noted similar regional blood flow patterns in panic disordered patients as in healthy controls with anticipatory anxiety, which calls into question whether abnormalities seen relate to structural differences or transient effects of anxiety (Reiman, Fusselman, et al., 1989; Reiman, Raichle, et al., 1989). Brain abnormalities such as these may lead to learning and memory deficits, if present in panic disordered individuals.

Individual studies have found associations between PD and a number of neuropsychological deficits, including executive function and episodic memory deficits (Airaksinen et al., 2005). However, many conflicting results have been produced, with some studies supporting memory deficits in PD (Asmundson et al., 1994; Lucas et al., 1991) and others reporting no memory problems of any kind (Gladsjo et al., 1998). No review was found of neuropsychological performance in PD. This paper aims to provide a systematic review of neuropsychological performance in PD compared to healthy control (HC) participants.

2.2 Methods

2.2.1 Search Strategy

Relevant studies published between January 1980 and March 2012 were identified by systematic searches of the PsycInfo, Embase, PsycArticles and Medline databases. Articles reporting neuropsychological performance of all anxiety disorder groups were initially identified, as a preliminary search of the literature indicated that PD groups were often used as comparison groups in studies that focused on other anxiety disorders, such as OCD (e.g. Purcell et al., 1998). Keywords for the search were “neurocognition”, “attention”, “executive function”, “learning”, “memory”, “inhibition” AND “neuropsychological tests” AND “anxiety”, “OCD”, “PTSD”. Terms were adapted and ‘exploded’ in keeping with subject headings for each database (see Appendix 2 for full search term list for each database). The reference lists of ten papers identified as appropriate after inclusion and exclusion criteria were applied, were checked for relevant studies, resulting in 3 additional papers. A ‘cited by’ search was conducted using Web of Science (1899-present) resulting in 2 additional papers. This resulted in 15 papers meeting study criteria. Subsequently two studies were discovered to be reporting on the same data (Lautenbacher et al., 2002; Sernal et al., 2003). The paper containing the most data was retained in the review, resulting in a total of 14 papers (Lautenbacher et al., 2002).

2.2.2 Inclusion and exclusion criteria

Studies were included if they reported on: (1) adults (18-65 years) (2) diagnosed with current PD according to DSM or ICD criteria (3) a comparison group of healthy controls (HC) (4) had ≥ 15 participants in each group and (5) were published in English. A relevant Spanish paper was found during the search but could not be included as it was only available in the Spanish language (Castillo et al., 2010). Studies on the effect of psychotropic medication or a treatment intervention were excluded. Investigations of cognitive performance in the presence of anxiety provoking words or stimuli were excluded. Studies of neuropsychological performance during brain imaging or brain activity recording were also excluded. The paper selection procedure is described in Figure 2.1, with a more detailed map in Appendix 3.

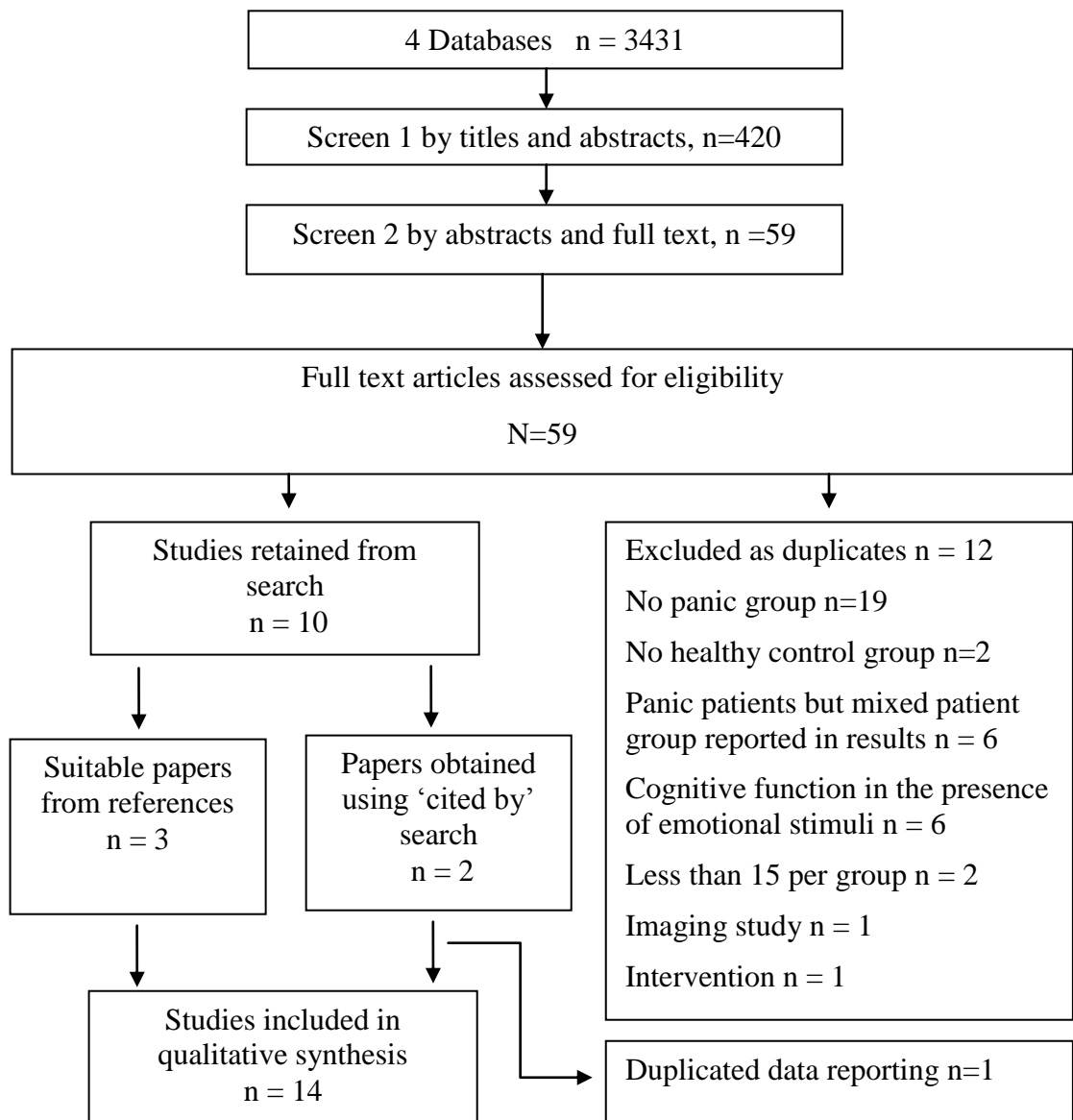


Figure 2.1 Flowchart showing search results, and the number of included and excluded studies.

2.2.3 Data Extraction

Data were extracted from each paper by the first author, according to a structured pro-forma covering key study characteristics. Data were extracted and compiled into Table 2.1.

2.2.4 Assessment of methodological quality

To rate the methodological quality of included studies, criteria were developed by the first author, drawing from the Cochrane Handbook for Systematic Review's guidance on assessing risk of bias (Higgins & Altman, 2008) and the Centre for Reviews and Dissemination (CRD) guidance on conducting quality assessment (CRD, 2008). A checklist of 8 quality criteria were identified a priori (Appendix 4). The ratings for the included studies are listed in Table 2.2. For each criterion, included studies were assigned one of four outcome ratings: 'well covered' (2 points); 'adequately addressed' (1 point); 'poorly addressed' or 'not addressed' (both 0 points). Two additional raters independently reviewed four studies each. Exact agreement was reached on 88% and 84% of the ratings respectively. A difference of one point occurred on 12.5% of the items and by 2 points on 1.5% items. Differences in rating of criteria were discussed and amended.

Table 2.1 Key Study Characteristics

Authors	Sample size^a	Groups matched on	Key exclusion criteria	Levels of anxiety compared between groups	Medication
Airaksinen et al. (2005)	33 PD (30 PD only and 3 Ag only) 175 HC ^b	age, education	No exclusions	No comparisons	No medications excluded
Asmundson et al. (1994)	18 PD 16 HC	gender, age, education	Current major depression and Social phobia excluded	BDI: PD > HC BAI: PD > HC	1 PD taking p.r.n. benzodiazepines
Boldrini et al. (2005)	15 PD with Ag 15 HC	gender, age, education handedness, intelligence	All Axis I or II excluded	No comparisons	Free from benzodiazepines (no time period) but SSRIs not excluded
Cavedini et al. (2002)	16 PD 34 HC ^b	gender, age, education	All Axis I or II excluded	No comparisons	All medication free for at least 2 weeks
Deckersbach et al. (2011)	20 PD 20 HC	gender, age, education	Depression, psychosis and bipolar disorder excluded	STAI: PD > HC BDI: PD > HC	All free from benzodiazepines for at least 4 weeks. One PD taking Sertraline
Galderisi et al. (2008)	28 PD (26 with Ag) 32 HC	gender, age, education handedness	MDD and other anxiety disorders excluded	No comparisons	Medication free for 4 weeks or drug naive
Gladysjo et al. (1998)	69 PD 19 HC	gender, age, education ethnicity, handedness	All Axis I or II excluded	No comparisons	Medication free for at least 2 weeks
Gordeev (2008)	93 PA 36 HC	education	No information	BDI: PD > HC STAI: PD > HC	Medication free for 2 weeks
Gorini et al. (2010)	31 PD with Ag, 31 HC	gender, age, education	Other primary diagnoses excluded	No comparisons	Medication free for 1-2 weeks

Table 2.1 Key Study Characteristics Continued

Authors	Sample size ^a	Groups matched on	Key exclusion criteria	Levels of anxiety compared between groups	Medication
Kaplan et al. (2006)	22 PD (11 PD only, 11 PD + MDD) ^c , 22 HC	gender, age, education	Other anxiety or depressive disorder excluded	MADRS: PD > HC Ham A: PD > HC	All medication free (no time period given)
Lautenbacher et al (2001)	21 PD, (16 with Ag, 5 without Ag) 20 HC ^b	gender	Lifetime comorbidity of Axis 1 excluded	No comparison	Medication free for 6 days
Lucas et al. (1991)	25 PD 25 HC	gender, age, education handedness	Current mood disorder, or other anxiety disorder excluded	BDI: PD > HC STAI: PD > HC	Patients remained on medication
Ludewig et al. (2003)	18 PD 35 HC ^b	gender, age	No information	No comparisons	14 of 18 PDs on medication including SSRIs and TCA
Purcell et al. (1998)	30 PD 30 HC ^b	gender, age, education handedness, IQ	Comorbid disorder excluded but anxiety or depression symptoms accepted	Ham D: PD = HC Ham A: PD > HC	19 PD on medication

a PD group is mixed with and without agoraphobia with details unavailable unless otherwise specified, *b* Additional groups were included in the study which did not form part of this review, *c* MDD is episode secondary to PD, STAI= State Trait Anxiety Inventory, TCA = tricyclic antidepressant, SSRI = selective serotonin reuptake inhibitor

Ag = agoraphobia, HamA = Hamilton Anxiety rating scales, HamD = Hamilton Depression rating scale, BDI= Beck Depression Inventory, BAI= Beck Anxiety Inventory, MADRS = Montgomery Asberg Depression Rating Scale

Table 2.2 Quality Criteria applied to Reviewed studies

Name of study	i exclusion criteria	ii group matching	iii diagnosis	iv neuropsychological measures	v sample size	vi uptake levels	vii outputs reported	viii stats used	Total
Airaksinen et al. (2005)	WC	AA	WC	AA	WC	AA	AA	AA	11
Asmundson et al. (1994)	WC	WC	WC	AA	AA	NA	AA	AA	10
Boldrini et al. (2005)	WC	WC	WC	WC	AA	NA	AA	AA	11
Cavedini et al. (2002)	AA	WC	WC	WC	AA	NA	AA	WC	11
Deckersbach et al. (2011)	AA	WC	WC	WC	AA	NA	AA	AA	10
Galderisi et al.(2008)	WC	WC	WC	AA	WC	NA	AA	AA	11
Gladsjo et al. (1998)	WC	WC	WC	WC	AA	AA	AA	AA	12
Gordeev (2008)	PA	PA	AA	AA	WC	NA	AA	WC	7
Gorini et al. (2010)	PA	WC	AA	AA	WC	NA	AA	AA	8
Kaplan et al. (2006)	WC	WC	WC	WC	AA	NA	AA	WC	12
Lautenbacher et al. (2001)	WC	AA	AA	AA	AA	NA	AA	AA	8
Lucas et al. (1991)	WC	WC	WC	WC	WC	NA	AA	AA	12
Ludewig et al. (2003)	PA	AA	WC	AA	AA	NA	PA	AA	6
Purcell et al. (1998)	WC	WC	WC	WC	WC	AA	AA	WC	14

i. Eligibility criteria are specified, ii. Comparison group is matched, iii. Diagnosis using appropriate criteria and measure, iv. Neuropsychological Measures are robust, v. Sample size adequate for all groups, vi. Levels of uptake are reported, vii. Results – appropriate outputs provided, viii. Appropriate Statistical techniques, WC=well covered, AA=adequately addressed, PA=poorly addressed, NA=not addressed

2.3 Results

2.3.1 Search results and characteristics of studies

From the search, 14 papers were identified comparing a PD group with a HC group. The 14 studies involved 439 patients with PD in total and 510 HCs (see Table 2.1 for details). The median sample size was 23.5 for PD patients (range 15 - 93) and 27.5 for HCs (range 15 - 175).

Three studies reported on the presence or absence of agoraphobia in their PD sample, but 11 did not. Both Boldrini et al. (2005) and Gorini et al. (2010) reported all PD participants to have PD with agoraphobia. Twenty six of the 28 PD participants in Galderisi et al.'s (2008) study had PD with agoraphobia.

2.3.2 Findings of the review

As many neuropsychological measures can be said to assess a number of cognitive functions, Lezak et al.'s (2004) categorisation of neuropsychological assessments has been broadly followed when tabulating and discussing the measures used in the reviewed studies. However, the category of executive functioning was expanded from that of Lezak et al. (2004) in line with Burgess (2003) to incorporate tests of inhibition, coordinated dual tasks (e.g. the Trail Making Task) and verbal fluency. In the context of the reviewed studies, such measures were used with the purpose of assessing executive functioning. Measures used in the reviewed studies and their reported results are detailed in Tables 2.3 to 2.6.

2.3.3 Memory

2.3.3.1 Verbal Memory

Short and long term verbal memory were investigated in eight studies using ten measures. Of these, four found poor performance in a PD group compared to HC and four did not find group differences.

Short term verbal memory was measured by five studies and impairment of PD patients compared to HC was reported in three studies. Two studies indicating a relative impairment of PD participants used non-standardised short term recall tasks

(Airaksinen et al., 2005; Gordeev, 2008) and the other used the California Verbal Learning Test (CVLT; Asmundson et al., 1994; Delis et al., 1987). The CVLT was used in two other studies, which did not report on performance of people with PD on short term memory scales (Deckersbach et al., 2011; Gladsjo et al., 1998). No differences between PD and HC groups were reported by Lucas et al. (1991) or Deckersbach et al. (2011) in measures of immediate recall of stories or paired words, taken from the Wechsler Memory Scale (WMS; Wechsler, 1987). Mixed results were reported in relation to cued short term memory, with deficits seen on a non-standardised task (Airaksinen et al., 2005) but not on the cued recall subscale of the CVLT (Asmundson et al., 1994). Overall, there was some support for impairment in short term memory when assessed by non-standardised measures but little support from standardised assessment.

Delayed verbal memory was investigated by seven studies. No differences were found between PD and HC groups on delayed verbal memory using the CVLT (Asmundson et al., 1994; Deckersbach et al., 2011; Gladsjo et al., 1998), the Auditory Verbal Learning Test (AVLT) (Galderisi et al., 2008), or the paired associates and logical memory subscales of the Wechsler Memory Scale (WMS) (Lucas et al., 1991). Using a selective reminding procedure (J. M. Fletcher, 1985), conflicting results were produced by two studies with Lucas et al. (1991) observing a deficit in long term verbal memory in a PD sample compared to HC while Boldrini et al. (2005) did not.

Table 2.3 Verbal memory in panic disorder compared to healthy controls

Verbal Memory Test	study/authors	PD v HC
CVLT		
immediate free recall trial 5	Asmundson et al. (1994)	↓
immediate free recall trial 1	Asmundson et al. (1994)	-
short delay free recall	Asmundson et al. (1994)	↓
total free recall	Asmundson et al. (1994)	↓
	Deckersbach et al. (2011)	-
	Gladso et al. (1998)	-
short delay cued recall	Asmundson et al. (1994)	-
retention	Asmundson et al. (1994)	-
	Deckersbach et al. (2011)	-
response inhibition	Asmundson et al. (1994)	-
response discrimination	Asmundson et al. (1994)	-
	Deckersbach et al. (2011)	-
	Gladso et al. (1998)	-
Word Lists		
AVLT delayed recall	Galderisi et al. (2008)	-
Warrington RMT	Gladso et al. (1998)	-
words remembered short term	Gordeev et al. (2008)	↓
words remembered		
Free recall	Airaksinen et al. (2005)	↓
Cued recall	Airaksinen et al. (2005)	↓
Hebb Digit Recurring test - accuracy index	Galderisi et al. (2008)	-
Buschke-Fuld Selective Reminding Test (SRT)		
long term recall	Boldrini et al. (2005)	-
long term storage	Boldrini et al. (2005)	-
intrusions	Boldrini et al. (2005)	-
delayed recall	Boldrini et al. (2005)	-
Verbal Selective Reminding Test (SRT)		
Long term storage	Lucas et al. (1991)	↓
trials to criterion	Lucas et al. (1991)	-
delayed recall	Lucas et al. (1991)	↓
long term retrieval	Lucas et al. (1991)	↓
Logical Memory (WMS)		
Delayed recall	Lucas et al. (1991)	-
immediate recall	Deckersbach et al. (2011)	-
Paired associate learning (WMS)		
Immediate recall	Lucas et al. (1991)	-
Delayed recall	Lucas et al. (1991)	-

↓Indicates significantly worse performance than HC

↑indicates significantly better performance than HC

- indicates no significant difference compared to HC

2.3.3.2 Visual Memory

Both short and long term visual memory in people with PD was investigated by eight studies using ten measures. Three studies reported deficits in people with PD compared to HC, while five reported no significant differences between these groups.

Short term visual memory was investigated in two studies, one using the Rey-Osterrieth Complex Figure test (RCFT; Rey, 1941) immediate recall scale (Deckersbach et al., 2011) and one using a non-standardised task, in which an array of numbers was visually presented followed by immediate recall (Gordeev, 2008). Both these tasks were associated with an impaired performance in people with PD compared to HC.

Seven studies reported on measures of long term visual memory, including measures of retention and recognition. Three studies used the Benton Visual Retention test (BVRT) (BVRT; Benton, 1945) with two of these reporting significantly worse long term visual memory in people with PD relative to HC (Asmundson et al., 1994; Deckersbach et al., 2011; Lucas et al., 1991). A selective reminding procedure (J. M. Fletcher, 1985) was used in two studies producing mixed results, as Lucas et al. (1991) reported poor performance in people with PD but this was not replicated by Gladsjo et al. (1998). Visual recognition memory was investigated using 3 subtests of the computerised Cambridge Neuropsychological Test Automated Battery (CANTAB; Cambridge Cognition, Cambridge, UK) and the Warrington Recognition Memory test (Faces)(Warrington, 1984). No differences were reported between PD and HC groups on these visual recognition tasks (Gladsjo et al., 1998; Kaplan et al., 2006; Purcell et al., 1998). People with PD also performed similarly to HC on the RCFT percent recall (Boldrini et al., 2005; Deckersbach et al., 2011), the Continuous Visual Memory test (Gladsjo et al., 1998; Trahan & Larrabee, 1989) and delayed recall of the Visual Reproduction subscale of the WMS (Lucas et al., 1991). These studies do not support a finding of difficulties in long term visual memory for people with PD.

In summary there is some support for a short term memory deficit in people with PD in both verbal and visual memory but the reliability and validity of a number of the

tasks providing this support is unclear. There is little support for impairment in either verbal or visual long term memory.

Table 2.4 Visual memory in panic disorder compared to healthy controls

Visual Memory Test	study/authors	HC
Benton Visual Retention Test		
Form F (BVRT-F)	Asmundson et al. (1994)	-
Errors	Deckersbach et al. (2011)	↓
Errors	Lucas et al. (1991)	↓
RCFT		
immediate recall	Deckersbach et al. (2011)	↓
percent recall	Boldrini et al. (2005)	-
percent recall	Deckersbach et al. (2011)	-
Visual Selective Reminding test (VSRT)		
long term storage	Gladso et al. (1998)	-
long term storage	Lucas et al. (1991)	↓
total recalled	Gladso et al. (1998)	-
long term retrieval	Gladso et al. (1998)	-
long term retrieval	Lucas et al. (1991)	↓
Delayed recall	Lucas et al. (1991)	↓
Trials to criterion	Lucas et al. (1991)	↓
Warrington RMT Faces	Gladso et al. (1998)	-
Continuous Visual Memory test (CVMT)		
total recalled	Gladso et al. (1998)	-
d-Prime	Gladso et al. (1998)	-
Numbers remembered, short term	Gordeev et al. (2008)	↓
Visual Reproduction (WMS) - delayed recall	Lucas et al. (1991)	↓
CANTAB		
Spatial Recognition Memory	Kaplan et al. (2006)	-
Spatial Recognition Memory	Purcell et al. (1998)	-
pattern recognition memory	Kaplan et al. (2006)	-
pattern recognition memory	Purcell et al. (1998)	-
Delayed match to sample	Kaplan et al. (2006)	-
Delayed match to sample	Purcell et al. (1998)	-

↓Indicates significantly worse performance than HC

↑indicates significantly better performance than HC

- indicates no significant difference compared to HC

2.3.4 Attention, perception and working memory

2.3.4.1 Working Memory

Working memory in people with PD was explored by seven studies using working memory span tasks. No difference between the performance of people with PD and HC were reported by four studies using the Digit Span (Wechsler, 1981) task. Two studies using the CANTAB computerised Spatial Span and Spatial Working Memory tasks also found no differences. Boldrini et al. (2005) and Galderisi et al. (2008) employed the Corsi Block Tapping Task (CBTT; Berch, 1998) to investigate working memory span, while Deckersbach et al. (2011) used the similar Spatial span task from the WMS (Wechsler, 1987). Performance was reported as no different to HC on measures of span (Boldrini et al., 2005; Deckersbach et al., 2011), however on the supraspan subscale, Boldrini et al. (2005) reported a poor learning process in spatial working memory in people with PD compared to HC. Galderisi and colleagues (2008) also administered the CBTT but only reported on the accuracy index, on which people with PD performed better than the HCs in their sample. In summary, there is very little support for working memory impairment in PD.

2.3.4.2 Attention

Attention was investigated in seven studies using six different tests. No impairments of people with PD were found compared to HC in any study (Airaksinen et al., 2005; Asmundson et al., 1994; Deckersbach et al., 2011; Galderisi et al., 2008; Gladsjo et al., 1998; Kaplan et al., 2006; Lucas et al., 1991).

2.3.4.3 Perception

Tests included in this section were classed primarily as tests of perception by Lezak et al. (2004) as they measure visual field perception, visual searching and facial recognition but also include selected and divided attention.

Four studies investigated these abilities in PD using six tasks. Poor performance was noted on three of these tasks. Individuals with PD performed poorly compared to HC on the Munsterberg Test, described as a test of selective attention and on a Schulte tables task of sustained attention (Gordeev, 2008). The Munsterberg test requires participants to find words in a random set of letters within a limited time. Psychometric properties for the Munsterberg task and Schulte tables were not found.

Some literature was found indicating that Schulte tables do not have well established psychometric properties (Ennok, 2010). In contrast to Gordeev's (2008) finding of poor selective attention, Lautenbacher et al. (2002) did not find overall group differences on selective attention using a computerised signal detection task. Divided attention was also explored by Lautenbacher et al. (2002) using a visual field neglect task in which individuals with PD demonstrated impaired performance relative to HC. Information on psychometric properties could not be found for Lautenbacher et al.'s (2002) measures. Facial recognition in the absence of a memory condition was assessed using the Benton Facial Recognition test (short form)(Benton, 1983), where the participant must identify photographs of the target person taken from different angles. Individuals with PD were as good at identifying faces as HCs (Boldrini et al., 2005). No difference in ability was seen between the two groups on a digit cancellation test (Asmundson et al., 1994). Overall, some support was found for impaired perceptual/attention abilities in people with PD but the reliability of the measures used was uncertain.

2.3.5 Visuospatial Ability

Visuospatial ability was investigated in PD by five studies using four measures. Three of these measures were standardised tasks - the Block Design task from the Wechsler Adult Intelligence Scale-Revised (WAIS-R), the copy task of the RCFT and the mental rotation task (Vandenberg & Kuse, 1978) and one a novel computer-based task (Jacobs et al., 1997). Two studies found no group differences in visuospatial ability using the RCFT copy score (Boldrini et al., 2005; Deckersbach et al., 2011). Poor visuospatial ability of people with PD was seen on the Block Design task by Asmundson et al. (1994) but was not replicated (Gladsjo et al., 1998). The ability to perform spatial rotations mentally was investigated by Deckersbach et al. (2011) using the mental rotation test. The PD group performed as well as HCs on this test. A virtual environment was used by Gorini et al. (2010) to investigate spatial orientation and learning in people with PD. Their study used a virtual water maze analogue where participants had to find the hidden platform in a virtual environment, starting from a different position at each trial. Learning the position of the platform over trials was impaired in the PD group compared to HCs, however this was a novel task which has not been standardised and high variability of

performance was noted in both groups. In summary, only one study provided support for visuospatial impairment in people with PD, using a novel non-standardised measure.

Table 2.5 Working memory in panic disorder compared to healthy controls

Cognitive function	Test	study/authors	PD v HC	
Working Memory	Digit span	Boldrini et al. (2005)	-	
		Deckersbach et al. (2011)	-	
		Gladso et al. (1998)	-	
		Lucas et al. (1991)	-	
	Corsi Block Tapping Task (CBT)			
	span	Boldrini et al. (2005)	-	
	supraspan	Boldrini et al. (2005)	↓	
	accuracy index	Galderisi et al. (2008)	↑	
	WMS-R			
	spatial span forward	Deckersbach et al. (2011)	-	
	spatial span backward	Deckersbach et al. (2011)	-	
	CANTAB			
	Spatial Span	Kaplan et al. (2006)	-	
Spatial Span	Purcell et al. (1998)	-		
Attention	Mental control task (WMS-R)	Deckersbach et al. (2011)	-	
		Lucas et al. (1991)	-	
	Continuous performance test	Galderisi et al. (2008)	-	
		TMT A	Airaksinen et al. (2005)	-
			Asmundson et al. (1994)	-
	Gladso et al. (1998)		-	
	Digit symbol (WAIS-R)	Galderisi et al. (2008)	-	
		Gladso et al. (1998)	-	
		Gladso et al. (1998)	-	
	Digit vigilance - time	Gladso et al. (1998)	-	
		Digit vigilance - errors	Gladso et al. (1998)	-
	CANTAB			
	Rapid Visual Information Processing	Kaplan et al. (2006)	-	
Perception	Digit Cancellation Test (DCT)	Asmundson et al. (1994)	-	
	Signal Detection (from Weiner-Test-System)	Lautenbacher et al. (2001)	-	
	Munsterberg test	Gordeev (2008)	↓	
			↓	
	Schulte tables	Gordeev (2008)		
	Visual Field Neglect task (from TAP)	Lautenbacher et al. (2001)	↓	
	Facial Recognition test (BFRT) short form	Boldrini et al. (2005)	-	
	Visuospatial ability	Block design (WAIS-R)	Asmundson et al. (1994)	↓
Gladso et al. (1998)			-	
Mental rotation test		Deckersbach et al. (2011)	-	
Spatial orientation and learning – virtual water maze analogue		Gorini et al. (2010)	↓	
RCFT				
Copy		Boldrini et al. (2005)	-	
Copy		Deckersbach et al. (2011)	-	

↓Indicates significantly worse performance than HC

↑indicates significantly better performance than HC

- indicates no significant difference compared to HC

2.3.6 Executive function

Executive function was assessed by nine studies using nine measures. Results were considered under the headings of set shifting, verbal fluency, decision making and planning and organising. Significant group differences were reported only on two measures.

2.3.6.1 Planning and Organising

People with PD demonstrated impaired performance relative to HC on the organisation score of the RCFT (Deckersbach et al., 2011). Purcell et al. (1998) administered the Tower of London task (CANTAB; Cambridge Cognition, Cambridge, UK) and found comparable performance between the two groups.

2.3.6.2 Set shifting

The set shifting performance of people with PD in comparison to HC was examined by six studies using five tasks. Individuals with PD performed as well as HC on the Wisconsin Card Sorting Task (WCST; Boldrini et al., 2005; Heaton et al., 1993). There were also no group differences found in both studies using the CANTAB intradimensional and extradimensional shifting task (Kaplan et al., 2006; Purcell et al., 1998). Three studies reported on the Trail Making Task B (TMT B; R. M. Reitan & Davidson, 1974), with only one (Airaksinen et al., 2005) reporting slower times in people with PD compared to HC.

2.3.6.3 Verbal Fluency

Five studies investigated letter fluency abilities, finding individuals with PD produced as many words as HCs. One of these also investigated category fluency (Benton, 1989; Gladsjo et al., 1998) and again found no group differences in number of words produced.

2.3.6.4 Decision Making

Decision Making ability was examined by Cavedini et al. (2002) using the Iowa Gambling Task (IGT; Bechara et al., 1994), by Kaplan et al. (2006) using the Cambridge Gambling task (Rogers et al., 1999) and by Ludewig et al. (2003) using a two-choice prediction task (Paulus, 1997). Performance of the PD group was not significantly different to the control group for any task, although PD participants showed increased sensitivity to error, being more likely to search for a better

responding strategy even at low error rates in Ludewig et al.'s (2003) study. Kaplan et al. (2006) reported that within their sample comorbid major depressive disorder (MDD) was associated with slow decision making.

In summary, the evidence reviewed does not support an executive function deficit in PD.

Table 2.6 Executive function in panic disorder compared to healthy controls

Cognitive function	Test	study/authors	PD v HC
Set shifting	TMT B	Airaksinen et al. (2005)	↓
		Asmundson et al. (1994)	-
		Gladso et al. (1998)	-
	WCST categories total errors perseverative errors non-p errors perseverative responses null sorts	Boldrini et al. (2005)	-
		Boldrini et al. (2005)	-
		Boldrini et al. (2005)	-
		Boldrini et al. (2005)	-
		Boldrini et al. (2005)	-
		Boldrini et al. (2005)	-
		Boldrini et al. (2005)	-
	CANTAB Intradimensional-Extradimensional Shift Total score IDS trial score EDS trial score Spatial working memory	Kaplan et al. (2006)	-
		Purcell et al. (1998)	-
		Purcell et al. (1998)	-
		Purcell et al. (1998)	-
		Purcell et al. (1998)	-
Planning and organising	Tower of London	Purcell et al. (1998)	-
	RCFT organisation	Deckersbach et al. (2011)	↓
verbal fluency	FAS in 60 sec FAS in 60 sec letter fluency COWAT category fluency	Airaksinen et al. (2005)	-
		Boldrini et al. (2005)	-
		Gladso et al. (1998)	-
		Deckersbach et al. (2011)	-
		Gladso et al. (1998)	-
Decision making	Iowa Gambling Task	Cavedini et al. (2002)	-
	Cambridge Gambling Task	Kaplan et al. (2006)	-
	Two-Choice Prediction Task	Ludewig et al. (2003)	-
	(Paulus et al., 1997)		

↓Indicates significantly worse performance than HC, ↑indicates significantly better performance than HC, - indicates no significant difference compared to HC

2.3.7 Summary of Neuropsychological findings

The findings of the reviewed studies suggest limited support for a short term memory deficit in people with PD in both verbal and visual memory, with five out of seven studies indicating a difference in performance. There is little support for impairment in perceptual ability, as although three out of four studies found differences, the reliability and validity of the measures used was unclear. Only three of fourteen studies found differences in long term memory compared to HC, which did not support long term memory impairment in PD. The findings reviewed did not indicate deficits in executive function, as only two of nine studies found group differences. Similarly, working memory was impaired only in one of seven studies and attention was not impaired in any of the seven studies incorporating tests of attention. Visuospatial abilities were impaired in two out of five studies, which does not suggest consistent impairment.

2.3.8 Assessment of Methodological Quality

Table 2.2 contains study ratings on the eight quality criteria selected. This rating system provides an indication of the relative methodological strengths of the studies reviewed, although it does not allow for detailed comparison.

Based on the chosen criteria, Purcell et al. (1998) was methodologically the strongest study, although the majority of studies were of average to high quality. Studies that reported significant results for more than half of the measures they utilised, tended to be of lower quality, as defined by the quality criteria. Four such studies (Airaksinen et al., 2005; Gorini et al., 2010; Lautenbacher et al., 2002; Lucas et al., 1991) failed to describe adjustment for the multiple comparisons they used. In addition, three of these studies (Airaksinen et al., 2005; Gorini et al., 2010; Lautenbacher et al., 2002) reported significant results on a measure for which no reliability or validity information was available. Gordeev (2008) used corrections for multiple comparisons and reported significant results for all the measures used, examining areas of perception and short term memory, however no reliability or validity data were available for any of these measures. These studies provided some of the support in favour of short term memory and perception difficulties in people with PD.

Studies which reported few significant differences associated with diagnosis of PD, tended to be of high quality as defined by the quality criteria. These studies (Asmundson et al., 1994; Boldrini et al., 2005; Deckersbach et al., 2011; Galderisi et al., 2008) reported significant differences between PD and HC participants for fewer than half of the measures they investigated. Although two (Asmundson et al., 1994; Galderisi et al., 2008) used one measure in their study that did not have reliability and validity data available, significant results were only reported on validated measures. These studies contributed findings supporting difficulties in short term memory, working memory span and learning, visuospatial abilities and executive function.

Four studies of high quality, as defined by the quality criteria, reported no significant differences between PD samples and HC (Cavedini et al., 2002; Gladsjo et al., 1998; Kaplan et al., 2006; Purcell et al., 1998). Three described no differences in relation to long term memory and set shifting (Gladsjo et al., 1998; Kaplan et al., 2006; Purcell et al., 1998); two in relation to decision making (Cavedini et al., 2002; Kaplan et al., 2006) and two relating to other aspects of executive functioning (Gladsjo et al., 1998; Purcell et al., 1998). One lower quality study also reported no significant findings on a decision making task for which no psychometric information was found (Ludewig et al., 2003). Studies with high methodological quality tended towards findings of little or no differences between PD and HC groups. However, three of the four high quality studies with negative findings had small sample sizes, reducing their power to detect differences.

Overall, within the studies reviewed, group matching, method of diagnosis and description of exclusion criteria were addressed adequately. Presentation of results was generally adequate, but all studies failed to provide confidence intervals or effect sizes with their results. Eight of the 14 studies reviewed reported sample sizes less than 25, indicating that they would have lacked the power to detect a large effect size with an alpha level of .05 in a 2-tailed comparison of two means (see Table 2.1). No studies described statistical power. Uptake levels were poorly reported or not addressed in all but three studies (Airaksinen et al., 2005; Gladsjo et al., 1998; Purcell et al., 1998). Eight studies reported corrections for multiple comparisons

(Asmundson et al., 1994; Boldrini et al., 2005; Cavedini et al., 2002; Deckersbach et al., 2011; Galderisi et al., 2008; Gordeev, 2008; Kaplan et al., 2006; Purcell et al., 1998). As most studies included a number of measures and various post hoc tests, the absence of correction for multiple comparisons is a potential confound. The lack of these corrections may have led to Type I errors in the four studies that did not address these corrections and reported significant results (Airaksinen et al., 2005; Gorini et al., 2010; Lautenbacher et al., 2002; Lucas et al., 1991).

No studies reported on the reliability and validity of the measures used, therefore these properties were further investigated. Most measures were described with psychometric properties in Lezak and colleagues' (2004) detailed description of neuropsychological assessment and were described as valid and reliable for the groups in question. However, six studies used a measure or measures not described in Lezak et al. (2004) and did not provide a reference to an appropriate source of reliability and validity data (Airaksinen et al., 2005; Asmundson et al., 1994; Galderisi et al., 2008; Gordeev, 2008; Gorini et al., 2010; Ludewig et al., 2003). One study used a measure from a German test battery, which had no reliability or validity data in English (Lautenbacher et al., 2002). An appropriate search for these data could not be performed in German due to translation difficulties.

2.4 Discussion

This systematic review examined the neuropsychological profile of individuals with panic disorder using the available literature. With only 14 studies included in the review, it demonstrates the scarcity of research in the area. The results obtained in these studies have mostly indicated an absence of difficulties in PD participants relative to HC, with no deficits being consistently reported across studies.

There was some support in the reviewed studies for potential deficits in short term verbal and visual memory in people with PD compared to HC. Results provided little support for impairment in any other area of neuropsychological function.

A number of factors may have influenced the obtained results, including methodological quality and characteristics of the sample used by each study, such as

the presence of comorbid disorders and the medication status of participants. These factors also affect the generalisability of the results.

Quality criteria were applied to the studies reviewed, in order to further evaluate the reported findings. Methodological strengths and weaknesses were highlighted. Key issues arising from the assessment of methodological quality were risk of Type I error by failing to correct for multiple comparisons and use of measures without evident reliability or validity data for this population. Considering only studies that did not suffer from these methodological weaknesses the overall profile changes very little: limited support remained for visual and verbal short term memory difficulties in people with PD (Asmundson et al., 1994; Deckersbach et al., 2011) but the lack of consistency of results does not support a conclusion of impairment in this area. No remaining studies supported verbal long term memory or perception deficits in people with PD, and only one of the five remaining studies reporting on visual long term memory provided support for deficits in that area (Deckersbach et al., 2011). This removal of the less methodologically robust studies did not change the overall findings of no group differences on tasks of working memory, attention, visuospatial ability and executive functioning.

As a number of Axis I and Axis II disorders have been associated with cognitive impairment (Trivedi, 2006), criteria allowing the inclusion of PD participants with comorbid disorders, may have impacted on the specificity of the findings. Eight studies reported having no comorbid disorders, two allowed all comorbidities, two excluded only depression and two did not clearly state their exclusions. Four out of five of those reporting no findings, excluded all comorbidities. The exclusion of comorbidities helps to isolate difficulties that are due to PD alone, without the influence of other psychological disorders. However, this also limits the generalisability of results, as in a typical clinical group, comorbidities are common. Within the reviewed studies, patients without comorbidity tended to perform similarly to HCs (Cavedini et al., 2002; Gladsjo et al., 1998; Kaplan et al., 2006; Purcell et al., 1998).

Half of the studies reviewed reported including participants on medication, although two of these excluded benzodiazepines. There were no trends in findings relating to

medication status of participants. This is somewhat surprising as benzodiazepines (Deckersbach et al., 2011) and tricyclic antidepressants (Stein & Strickland, 1998) have been associated with additional cognitive impairment while SSRIs have not been consistently associated with impairment (Mataix-Cols et al., 2002).

Ten of the fourteen studies matched groups on age, gender and education. Of the four poorly matched groups, three of these were among those who produced a high number of significant findings. Poor group matching at the outset may have influenced results, as differences in age, gender and education have been shown to impact on neuropsychological test performance (Corral et al., 2006; Lowe et al., 2003; Reitan & Wolfson, 1995).

State anxiety at the time of testing was measured in eleven of fourteen studies. Eight of these made comparisons between PD and HC groups. In these studies, statistical tests suggested that PD groups were more anxious than HC at the time of testing. There was no pattern in the data relating to participant groups identified as being more anxious subsequently performing worse on tasks. However, as higher levels of anxiety were consistent among PD patients where it was reported, it is likely that this was also the case in studies where comparisons were not made between PD and HC groups. Literature suggests that state anxiety is unlikely to impact on test performance but it has suggested that those with lower IQ tend to be more anxious in advance of testing (Gass & Curiel, 2011).

2.4.1 Limitations

Only papers written in English were included in this review, limiting its scope. At least one potentially relevant study, not published in English, was excluded (Castillo et al., 2010). Studies containing PD samples of less than 15 were excluded from the review. This also reduced the number of studies reviewed, however the statistical power of such studies would have been low and findings, particularly negative findings, would have been difficult to interpret (Bezeau & Graves, 2001). This review is based on a relatively small number of studies, however this is primarily due to the scarcity of literature rather than the exclusion of potentially relevant studies. The consistency of the findings across these studies allows for greater confidence in conclusions drawn from this small number of studies.

2.4.2 Recommendation/implication for future research

These studies seem to suggest no consistent cognitive deficits in individuals with PD, which is in keeping with similar findings in populations with Social Phobia and Generalised Anxiety Disorder (Airaksinen et al., 2005; O'Toole & Pedersen, 2011). As such, neuropsychological functioning is unlikely to impact significantly on clinical practice in the treatment of PD. An impairment in short term memory, if it were present in some PD patients, may impact on the psychoeducation phase of CBT treatment, as recommended by the National Institute of Health and Clinical Excellence (NICE, 2011). The provision of written materials and other memory aids could potentially be helpful.

Future research should consider using sample sizes appropriate to detecting medium to large effect sizes and reporting on the effect sizes obtained, in order to further illustrate the potential magnitude of any differences detected (Bezeau & Graves, 2001). Specific hypotheses focussing on the highlighted areas of potential impairment, particularly short term memory, with an effort to use the same or directly comparable measures to other studies, would contribute to the clarification of findings. In addition, the specificity of any potential impairment requires further examination. While PD has been compared to OCD on a number of occasions (Bannon et al., 2006), comparisons with disorders such as Social Phobia and GAD, which have demonstrated similar patterns of neuropsychological performance, may help to illustrate if there are any specific impairments related to PD.

2.4.3 Conclusion

This systematic review of the neuropsychological profile of Panic Disorder (PD) demonstrates that within the current literature there is little support for any neuropsychological impairment in PD. Some support was found for an impairment in short term memory, which requires further investigation using larger sample sizes (25 or more) in order to detect large effect sizes ($d=0.8$) using the parameters of a power of 80% and a 0.05 two tailed significance level. The use of appropriate clinical comparison groups to determine the specificity of any impairment found is also recommended.

2.5 References

- Airaksinen, E., Larsson, M., Forsell, Y., 2005. Neuropsychological functions in anxiety disorders in population-based samples: evidence of episodic memory dysfunction. *J. Psychiatr. Res.* 39, 207-214.
- American Psychiatric Association, 2000. *Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-TR, 4th Edition, Text Revision*. American Psychiatric Press, Inc., Washington, DC.
- Asmundson, G.J., Stein, M.B., Larsen, D.K., Walker, J.R., 1994. Neurocognitive function in panic disorder and social phobia patients. *Anxiety* 1, 201-207.
- Baillie, A.J., Rapee, R.M., 2005. Panic attacks as risk markers for mental disorders*. *Soc. Psychiatry Psychiatr. Epidemiol.* 40, 240-244.
- Bannon, S., Gonsalvez, C.J., Croft, R.J., Boyce, P.M., 2006. Executive functions in obsessive-compulsive disorder: state or trait deficits? *Aust. N. Z. J. Psychiatry* 40, 1031-1038.
- Bechara, A., Damasio, A.R., Damasio, H., Anderson, S.W., 1994. Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition* 50, 7-15.
- Beck, A.T., Clark, D.A., 1997. An information processing model of anxiety: automatic and strategic processes. *Behav. Res. Ther.* 35, 49-58.
- Benton, A.L., 1945. A visual retention test for clinical use. *Archives of Neurology And Psychiatry* 54, 212-216.
- Benton, A.L., 1983. *Contributions to neuropsychological assessment*. Oxford University Press, New York.
- Benton, A.L., 1989. *Multilingual aphasia examinations*. AJA Associates, Iowa City, IA.
- Berch, D., 1998. The Corsi Block-tapping Task: methodological and theoretical considerations. *Brain Cogn.* 38, 317-338.
- Bezeau, S., Graves, R., 2001. Statistical power and effect sizes of clinical neuropsychology research. *J. Clin. Exp. Neuropsychol.* 23, 399-406.
- Bisaga, A., Katz, J.L., Antonini, A., Wright, C.E., Margouleff, C., Gorman, J.M., Eidelberg, D., 1998. Cerebral glucose metabolism in women with panic disorder. *Am J Psychiatry* 155, 1178-1183.
- Boldrini, M., del Pace, L., Placidi, G., Keilp, J., Ellis, S., Signori, S., Cappa, S., 2005. Selective cognitive deficits in obsessive-compulsive disorder compared to panic disorder with agoraphobia. *Acta Psychiatr. Scand.* 111, 150-158.

- Bouton, M.E., Mineka, S., Barlow, D.H., 2001. A modern learning theory perspective on the etiology of panic disorder. *Psychol. Rev.* 108, 4-32.
- Burgess, P.W., 2003. Assessment of executive function, In: Halligan, P.W., Kischka, U., Marshall, J.C. (Eds.), *Handbook of Clinical Neuropsychology*. Oxford University Press, Oxford; New York.
- Castillo, E.P., Coy, P.E.C., Shejet, F.O., Duran, E.T., Cabrera, D.M., 2010. Cognitive function evaluation: attention and memory in panic disorder patients. *Salud Mental* 33, 481-488.
- Cavedini, P., Riboldi, G., D'Annunzi, A., Belotti, P., Cisima, M., Bellodi, L., 2002. Decision-making heterogeneity in obsessive-compulsive disorder: Ventromedial prefrontal cortex function predicts different treatment outcomes. *Neuropsychologia* 40, 205-211.
- Cavedini, P., Zorzi, C., Bassi, T., Gorini, A., Baraldi, C., Ubbiali, A., Bellodi, L., 2006. Decision-making functioning as a predictor of treatment outcome in anorexia nervosa. *Psychiatry Res.* 145, 179-187.
- Clark, D.M., 1986. A cognitive approach to panic. *Behav. Res. Ther.* 24, 461-470.
- Clark, D.M., Salkovskis, P.M., Oest, L.-G., Breitholz, E., Koehler, K.A., Westling, B.E., Jeavons, A., Gelder, M., 1997. Misinterpretation of body sensations in panic disorder. *J. Consult. Clin. Psychol.* 65, 203-213.
- Corral, M., Rodriguez, M., Amenedo, E., Sanchez, J.L., Diaz, F., 2006. Cognitive Reserve, Age, and Neuropsychological Performance in Healthy Participants. *Developmental Neuropsychology* 29, 479-491.
- CRD, 2008. CRD's guidance for undertaking reviews in health care. Centre for Reviews and Dissemination, University of York.
- Deckersbach, T., Moshier, S.J., Tuschen-Caffier, B., Otto, M.W., 2011. Memory Dysfunction in Panic Disorder: An Investigation of the Role of Chronic Benzodiazepine Use. *Depress. Anxiety* 28, 999-1007.
- Delis, D.C., Kramer, J.H., Kaplan, E., Ober, B.A., 1987. *California Verbal Learning Test*. The Psychological Corporation, New York.
- Ehlers, A., Margraf, J., Davies, S., Roth, W.T., 1988. Selective processing of threat cues in subjects with panic attacks. *Cognition and Emotion* 2, 201-219.
- Ennok, N., 2010. The Untested Assumptions of Schulte Tables, The International Neuropsychological Society, The Polish Neuropsychological Society and The Polish Neuroscience Society Joint Mid-Year Meeting, Krakow. Poland.
- Fletcher, J.M., 1985. Memory for Verbal and Nonverbal Stimuli in Learning Disability Subgroups: Analysis by Selective Reminding. *J. Exp. Child Psychol.* 40, 244-259.

- Galderisi, S., Mancuso, F., Mucci, A., Garramone, S., Zamboli, R., Maj, M., 2008. Alexithymia and cognitive dysfunctions in patients with panic disorder. *Psychother. Psychosom.* 77, 182-188.
- Gass, C.S., Curiel, R.E., 2011. Test Anxiety in Relation to Measures of Cognitive and Intellectual Functioning. *Archives of Clinical Neuropsychology* 26, 396-404.
- Gladysjo, J.A., Rapaport, M.H., McKinney, R., Lucas, J.A., Rabin, A., Oliver, T., Davis, J., Auerbach, M., Judd, L.L., 1998. A neuropsychological study of panic disorder: Negative findings. *J. Affect. Disord.* 49, 123-131.
- Gordeev, S.A., 2008. Cognitive functions and the state of nonspecific brain systems in panic disorders. *Neuroscience & Behavioral Physiology* 38, 707-714.
- Gorini, A., Schruers, K., Riva, G., Griez, E., 2010. Nonhomogeneous results in place learning among panic disorder patients with agoraphobia. *Psychiatry Res.* 179, 297-305.
- Hagenaars, M.A., van Minnen, A., Hoogduin, C.A.L., Verbraak, M., 2009. A transdiagnostic comparison of trauma and panic memories in PTSD, panic disorder, and healthy controls. *J. Behav. Ther. Exp. Psychiatry* 40, 412-422.
- Heaton, R.K., Chelune, G.J., Talley, J.L., Kay, G.G., Curtiss, G., 1993. *Wisconsin Card Sorting Test Manual: Revised and Expanded.* . Psychological Assessment Resources Inc, Florida.
- Higgins, J., Altman, D., 2008. Chapter 8: Assessing risk of bias in included studies., In: Higgins, J., Green, S. (Eds.), *Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.1 (updated September 2008).* . The Cochrane Collaboration, 2008. Available from www.cochrane-handbook.org.
- Jacobs, W.J., Laurance, H.E., Thomas, K.G.F., 1997. Place Learning in Virtual Space I: Acquisition, Overshadowing, and Transfer. *Learn. Motiv.* 28, 521-541.
- Kaplan, J.S., Erickson, K., Luckenbaugh, D.A., Weiland-Fiedler, P., Geraci, M., Sahakian, B.J., Charney, D., Drevets, W.C., Neumeister, A., 2006. Differential performance on tasks of affective processing and decision-making in patients with Panic Disorder and Panic Disorder with comorbid Major Depressive Disorder. *J. Affect. Disord.* 95, 165-171.
- Kessler, R.C., Chiu, W.T., Jin, R., Ruscio, A.M., Shear, K., Walters, E.E., 2006. The epidemiology of panic attacks, panic disorder, and agoraphobia in the National Comorbidity Survey Replication. *Arch. Gen. Psychiatry* 63, 415-424.
- Lautenbacher, S., Sernal, J., Krieg, J.C., 2002. Divided and selective attention in panic disorder. A comparative study of patients with panic disorder, major depression and healthy controls. *Eur. Arch. Psychiatry Clin. Neurosci.* 252, 210-213.

Lezak, M.D., Howieson, D.B., Loring, D.W., 2004. *Neuropsychological Assessment* 4th Edition. Oxford University Press, New York.

Lowe, P.A., Mayfield, J.W., Reynolds, C.R., 2003. Gender differences in memory test performance among children and adolescents. *Archives of Clinical Neuropsychology* 18, 865-878.

Lucas, J.A., Telch, M.J., Bigler, E.D., 1991. Memory functioning in panic disorder: A neuropsychological perspective. *J. Anxiety Disord.* 5, 1-20.

Ludewig, S., Paulus, M.P., Ludewig, K., Vollenweider, F.X., 2003. Decision-making strategies by panic disorder subjects are more sensitive to errors. *J. Affect. Disord.* 76, 183-189.

Lundh, L.G., Wikstrom, J., Westerlund, J., Ost, L.G., 1999. Preattentive bias for emotional information in panic disorder with agoraphobia. *J. Abnorm. Psychol.* 108, 222-232.

Martinez-Gonzalez, A.E., Piqueras-Rodriguez, J.A., 2008. Neuropsychological update on obsessive-compulsive disorder. *Rev. Neurol.* 46, 618-625.

Mataix-Cols, D., Alonso, P., Pifarré, J., Menchón, J.M., Vallejo, J., 2002. Neuropsychological performance in medicated vs. unmedicated patients with obsessive-compulsive disorder. *Psychiatry Res.* 109, 255-264.

Mataix-Cols, D., van den Heuvel, O.A., 2006. Common and distinct neural correlates of obsessive-compulsive and related disorders. *Psychiatr. Clin. North Am.* 29, 391-410.

Menzies, L., Chamberlain, S.R., Laird, A.R., Thelen, S.M., Sahakian, B.J., Bullmore, E.T., 2008. Integrating evidence from neuroimaging and neuropsychological studies of obsessive-compulsive disorder: The orbitofronto-striatal model revisited. *Neurosci. Biobehav. Rev.* 32, 525-549.

Millan, M.J., Agid, Y., Brüne, M., Bullmore, E.T., Carter, C.S., Clayton, N.S., Connor, R., Davis, S., Deakin, B., DeRubeis, R.J., Dubois, B., Geyer, M.A., Goodwin, G.M., Gorwood, P., Jay, T.M., Joëls, M., Mansuy, I.M., Meyer-Lindenberg, A., Murphy, D., Rolls, E., Saletu, B., Spedding, M., Sweeney, J., Whittington, M., Young, L.J., 2012. Cognitive dysfunction in psychiatric disorders: characteristics, causes and the quest for improved therapy. *Nat Rev Drug Discov* 11, 141-168.

NICE, 2011. Generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults. NICE clinical guideline 113.

O'Toole, M.S., Pedersen, A.D., 2011. A systematic review of neuropsychological performance in social anxiety disorder. *Nordic Journal of Psychiatry* 65, 147-161.

Olley, A., Malhi, G., Sachdev, P., 2007. Memory and executive functioning in obsessive-compulsive disorder: A selective review. *J. Affect. Disord.* 104, 15-23.

Paulus, M.P., 1997. Long-range interactions in sequences of human behavior. *Phys. Rev. E* 55.

Phan, K.L., Orlichenko, A., Boyd, E., Angstadt, M., Coccaro, E.F., Liberzon, I., Arfanakis, K., 2009. Preliminary Evidence of White Matter Abnormality in the Uncinate Fasciculus in Generalized Social Anxiety Disorder. *Biol. Psychiatry* 66, 691-694.

Purcell, R., Maruff, P., Kyrios, M., Pantelis, C., 1998. Neuropsychological deficits in obsessive-compulsive disorder: a comparison with unipolar depression, panic disorder, and normal controls. *Arch. Gen. Psychiatry* 55, 415-423.

Reiman, E.M., Fusselman, M.J., Fox, P.T., Raichle, M.E., 1989a. Neuroanatomical Correlates of Anticipatory Anxiety. *Science* 243, 1071-1074.

Reiman, E.M., Raichle, M.E., Robins, E., Mintun, M.A., Fusselman, M.J., Fox, P.T., Price, J.L., Hackman, K.A., 1989b. Neuroanatomical Correlates of a Lactate-Induced Anxiety Attack. *Arch. Gen. Psychiatry* 46, 493-500.

Reitan, R.M., Davidson, L.A., 1974. *Clinical neuropsychology: current status and applications*. Wiley, New York.

Reitan, R.M., Wolfson, D., 1995. Influence of age and education on neuropsychological test results. *The Clinical Neuropsychologist* 9, 151-158.

Rey, A., 1941. L'examen psychologique dans les cas d'encephalopathie traumatique.(Les problems.). *Archives de Psychologie* 28, 215-285.

Rogers, R., Everitt, B., Baldacchino, A., Blackshaw, A., Swainson, R., Wynne, K., Baker, N., Hunter, J., Carthy, T., Booker, E., London, M., Deakin, J., Sahakian, B., Robbins, T., 1999. Dissociable deficits in the decision-making cognition of chronic amphetamine abusers, opiate abusers, patients with focal damage to prefrontal cortex, and tryptophan-depleted normal volunteers: Evidence for monoaminergic mechanisms. *Neuropsychopharmacology* 20, 322-339.

Spernal, J., Krieg, J.C., Lautenbacher, S., 2003. Pain thresholds as a putative functional test for cerebral laterality in major depressive disorder and panic disorder. *Neuropsychobiology* 48, 146-151.

Stein, R.A., Strickland, T.L., 1998. A Review of the Neuropsychological Effects of Commonly Used Prescription Medications. *Archives of Clinical Neuropsychology* 13, 259-284.

Szeszko, P.R., Ardekani, B.A., Ashtari, M., Malhotra, A.K., Robinson, D.G., Bilder, R.M., Lim, K.O., 2005. White matter abnormalities in obsessive-compulsive disorder: a diffusion tensor imaging study. *Arch. Gen. Psychiatry* 62, 782-790.

Tabarés-Seisdedos, R., Balanzá-Martínez, V., Sánchez-Moreno, J., Martínez-Aran, A., Salazar-Fraile, J., Selva-Vera, G., Rubio, C., Mata, I., Gómez-Beneyto, M., Vieta, E.,

2008. Research report: Neurocognitive and clinical predictors of functional outcome in patients with schizophrenia and bipolar I disorder at one-year follow-up. *J. Affect. Disord.* 109, 286-299.

Tchanturia, K., Davies, H., Lopez, C., Schmidt, U., Treasure, J., Wykes, T., 2008. Neuropsychological task performance before and after cognitive remediation in anorexia nervosa: a pilot case-series. *Psychol. Med.* 38, 1371-1373.

Teachman, B.A., Smith-Janik, S.B., Saporito, J., 2007. Information processing biases and panic disorder: relationships among cognitive and symptom measures. *Behav. Res. Ther.* 45, 1791-1811.

Trahan, D.E., Larrabee, G.J., 1989. Continuous Visual Memory Test. Psychological Assessment Resources, Odessa, FL.

Trivedi, J.K., 2006. Cognitive deficits in psychiatric disorders: Current status. *Indian Journal Of Psychiatry* 48, 10-20.

van den Heuvel, O.A., Veltman, D.J., Groenewegen, H.J., Witter, M.P., Merkelbach, I., Cath, D.C., van Balkom, A., van Oppen, P., van Dyck, R., 2005. Disorder-specific neuroanatomical correlates of attentional bias in obsessive-compulsive disorder, panic disorder, and hypochondriasis. *Arch. Gen. Psychiatry* 62, 922-933.

Vandenberg, S.G., Kuse, A.R., 1978. Mental rotations, a group test of three-dimensional spatial visualization. *Percept. Mot. Skills* 47, 599-604.

Vythilingam, M., Anderson, E.R., Goddard, A., Woods, S.W., Staib, L.H., Charney, D.S., Bremner, J.D., 2000. Temporal lobe volume in panic disorder - a quantitative magnetic resonance imaging study. *Psychiatry Res.-Neuroimaging* 99, 75-82.

Warrington, E.K., 1984. Recognition Memory Test. NFER-Nelson, Windsor, UK.

Wechsler, D., 1981. Wechsler Adult Intelligence Scale-Revised (WAIS-R). The Psychological Corporation.

Wechsler, D., 1987. Wechsler Memory Scale-Revised Manual. The Psychological Corporation, San Antonio, TX.

Chapter 3: Bridging Chapter

As the introduction of the journal article is necessarily brief and focused on only the thesis aims covered in the article, additional introductory information is necessary to describe the areas covered by the additional data analysis conducted outside the scope of the journal article.

3.1 The Cognitive Model of Bulimia Nervosa

Fairburn *et al.*'s (2003) cognitive behavioural model of BN implicates a dysfunctional system for evaluating self worth as a central maintaining mechanism. They propose that sufferers evaluate themselves based on eating, shape and weight and on their ability to control them. They further suggest that, in certain patients, one or more of four additional maintaining mechanisms operate. These additional mechanisms are severe perfectionism, core low self esteem, mood intolerance and interpersonal difficulties. Fairburn *et al.* (2003) broadened this model of BN into a transdiagnostic theory of eating disorders, emphasising the similarities between eating disorders. They highlighted the fact that individuals will often move between diagnostic categories over time and suggested that the maintaining mechanisms proposed for BN are common to all eating disorders. As key maintaining factors relate to maladaptive cognitive processes, neuropsychological research has investigated whether there are similar patterns of neuropsychological impairment in BN as have been observed in AN.

Beyond the neuropsychological focus of the current study, additional data were collected relating to maintaining factors proposed for BN. The primary maintaining mechanism of dysfunctional evaluation of eating, weight and shape, was measured by the Eating Disorder Examination, a semi structured interview described further in the Methods chapter. Obsessive compulsive symptoms in BN, and their relation to neuropsychological performance were also addressed in the study. Obsessive compulsive symptoms are common in BN and are linked to the construct of perfectionism (Egan *et al.*, 2011; Tchanturia, Morris, *et al.*, 2004). Obsessive compulsive symptoms were measured using both the Yale-Brown Obsessive Compulsive Scale (YBOCS) and the Obsessive Compulsive scale of the Symptom

Checklist 90-Revised (SCL-90-R). Core low self esteem was addressed using the Self Liking/Self Competence scale and aspects of interpersonal difficulties were addressed using the Social Problem Solving Inventory (SPSI) and the interpersonal sensitivity scale of the SCL-90-R. The Self Liking/Self Competence scale and the Social Problem Solving Inventory are not included in the journal article and are introduced below.

3.1.1 The Self liking/ Self Competence scale (Tafarodi & Swann, 2001)

The Self liking/Self Competence scale was developed by Tafarodi and colleagues (Tafarodi & Milne, 2002; Tafarodi & Swann, 2001) based on theoretical research using factor analysis of Rosenberg's (1965) self esteem scale. The concept of self esteem used in Rosenberg's scale, is a one-dimensional construct that taps into the 'self worth' element of self esteem. Tafarodi and Milne (2002) identified two separate dimensions of self-esteem, namely self liking and self competence. Self liking taps into the 'self worth' element of self esteem, while self competence relates to an individual's perception of their ability to deal with challenges.

Low self esteem is considered to be a core element in eating disorder theory and treatment (Fairburn *et al.*, 2003). It has also been associated with anxiety and depression in community and eating disordered samples (Ackard *et al.*, 2011; Rosenberg, 1962; Takagishi *et al.*, 2011). Self esteem, as measured by the Self Liking/Self Competence scale (Tafarodi & Swann, 2001) has been noted in the literature to be significantly lower in anorexic patient groups than in healthy controls (Paterson *et al.*, 2007). Self competence has been significantly associated with increased perfectionism and interpersonal distrust in anorexia nervosa (AN), and changes in self liking and self competence have been associated with changes in eating disordered behaviours in both AN and BN (Gordon *et al.*, 2005; Surgenor *et al.*, 2007). This research suggests that self liking and self competence may be important factors in the development or maintenance of eating disorders.

3.1.2 Social Problem Solving Inventory (SPSI) (D'Zurilla *et al.*, 2002)

Social problem solving has been proposed by D'Zurilla and Maydeu-Olivares (1995) to result from maladaptive cognitive processes and to be a risk factor for psychological disorder. They describe social problem solving as a multidimensional

construct relating to adaptive orientation towards problems and the use of effective problem solving strategies. The dimensions identified by the Social Problem Solving Inventory are Positive Problem Orientation, Negative Problem Orientation, Rational Problem Solving, Impulsivity/Carelessness style and Avoidance style.

Although interpersonal difficulties are considered to be important in BN (Fairburn *et al.*, 2003), and interpersonal therapy has been found to be as effective for BN as Cognitive-Behavioural Therapy in the long term (Agras *et al.*, 2000), no research is available investigating social problem solving in BN. However, the existing literature indicates that social problem solving is impaired in individuals with eating disorders (Paterson *et al.*, 2011; Swanson *et al.*, 2010). McFillin (2009) found that adolescents with an eating disorder demonstrated more hostile attributional biases and experienced a significantly greater intensity of negative emotions when presented with vignettes of social dilemmas than did healthy controls. Svaldi *et al.* (2011) found that women with binge eating disorder produced less effective social problem solving strategies than healthy controls. Using the SPSI, anorexic individuals have been found to show a significantly higher negative problem orientation than controls and to demonstrate impulsive and avoidant problem solving styles (Paterson *et al.*, 2011; Swanson *et al.*, 2010).

Anxiety and depression symptoms have also been associated with poor problem solving in non-clinical populations (Haaga *et al.*, 1995; Haugh, 2006) and in clinical populations, such as the anxiety disorder group reported on by Abbass and Mohammad (2008). This clinical group consisted of OCD, PTSD and panic disorder patients, who demonstrated higher negative problem orientation, impulsivity/carelessness style and avoidance style than healthy controls. In a mixed clinical group with at least one Axis I disorder, patients were also found to use poor social problem solving relative to healthy controls (Bray *et al.*, 2007). Poor social problem solving has been found to correlate with both impulsivity (McMurran *et al.*, 2002) and perfectionism (Chang, 2002), and has been suggested to be associated with the orbitofrontal regions of the brain (Hanten *et al.*, 2011).

3.1.3 Impulsivity

Impulsivity is another feature of BN that has been investigated in the literature (Waxman, 2009). This characteristic most commonly takes the form of bingeing behaviours, but bulimia is also associated with higher rates of shoplifting, substance abuse and self harm (Goldner *et al.*, 2000; Hudson *et al.*, 2007; Ruuska *et al.*, 2005). Impulsive behaviours in BN may be a reflection of underlying cognitive deficits in inhibition (Engel *et al.*, 2005; Kemps & Wilsdon, 2010; Kirisci *et al.*, 2004; Rosval *et al.*, 2006; Verdejo-García *et al.*, 2006). In relation to this, Robinson *et al.* (2009) have proposed a model of impulsivity in bulimia where the effect of trait impulsivity is moderated by cognitive inhibition skills. They suggest that temperamental impulsivity is a risk factor for impulsive behaviour, but that temperamental impulsivity can be overcome by good cognitive inhibition. They propose that training in cognitive control could be helpful to eating disordered individuals high in impulsive behaviours. Levels of impulsivity may also have implications for recovery, with lower levels of impulsivity associated with better treatment outcomes in BN (Castellini *et al.*, 2012).

3.2 Composition of the Patient groups used in this study

Selection criteria for the groups included in this study were chosen to allow a clinically representative sample of each disorder group. The comparison group was selected on the basis of being in treatment for anxiety and/or depression in the Adult Psychological Therapies Service in Tayside, and scoring in the moderate to severe range on either of the anxiety or depression subscales of the Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983).

The BN group included any patients in treatment for bulimia nervosa - both patients diagnosed with Bulimia Nervosa and also those diagnosed with Eating Disorder Not Otherwise Specified - Bulimic type (EDNOS-BN). National Institute for Health and Clinical Excellence (NICE, 2004a) guidelines for the treatment of eating disorders recommend that treatment of EDNOS be conducted using the same model as the disorder it most closely resembles. Therefore, patients with EDNOS-BN are routinely treated in the same way as those with BN. This is similar to the inclusion

criteria for bulimic groups used in other studies (Bara-Carril *et al.*, 2004; Schmidt *et al.*, 2006). Different diagnostic systems were in use in the Tayside and Grampian Eating Disorder Services, therefore the ICD 10 diagnostic categories of BN and Atypical BN (excluding Binge Eating disorder) were applied (WHO, 2010). These are comparable to the DSM-IV-TR diagnoses of BN and EDNOS-BN.

The category of EDNOS exists in DSM-IV-TR to describe patients who do not meet all the criteria for BN or AN diagnoses, while ICD 10 includes categories of 'Atypical Anorexia', 'Atypical Bulimia' and 'Eating Disorder Unspecified' for this purpose. Recent studies have reported forty to sixty percent of those seeking treatment for eating disorders falling within the EDNOS category when using DSM-IV-TR criteria, making them an important patient group in eating disorder research (Button *et al.*, 2005; Fairburn *et al.*, 2007; Ricca *et al.*, 2001; Rockert *et al.*, 2007). Differences between patients with BN and EDNOS-BN on measures of eating pathology and general psychopathology have been found to be non-significant (Garfinkel *et al.*, 1995; Martin *et al.*, 2000; Ricca *et al.*, 2001; Tobin *et al.*, 1997).

3.2.1 Gender of Participants

Both groups contained only female participants. This was decided in order to be comparable to the majority of the current literature relating to BN (Alvarez-Moya *et al.*, 2009; Brand *et al.*, 2007; Kemps & Wilsdon, 2010; Rosval *et al.*, 2006; Van den Eynde *et al.*, 2012). Male patients have been excluded from many recent eating disorder studies, due to the low numbers that present for treatment and the gender differences that have been found in the literature on eating disorders. The literature suggests that significantly fewer males suffer from eating disorders than females (Hudson *et al.*, 2007; Treasure *et al.*, 2010). In a large population study in the United States, a 0.5% lifetime prevalence of BN was reported among males compared to 1.5% among females and a 12 month prevalence of 0.1% in males compared to 0.5% in females (Hudson *et al.*, 2007). In addition, proportions of males attending for treatment of bulimia, as represented in current literature, are of the order of 5-10% of consecutive referrals (Fairburn *et al.*, 2007; Mehler *et al.*, 2008; Zeeck *et al.*, 2007). Differences between males and females with bulimia in relation to age of onset, premorbid obesity, homosexuality and concern with weight control have been reported in the literature although very few studies have reported on gender

differences (Carlat & Camargo Jr, 1991). As the literature suggests that there may be differences between male and female patients with bulimia, and that few male patients are likely to be available for participation, it was decided to include only female patients. This also allows the study sample to be directly comparable to existing key papers that have used only female participants.

3.3 Research Links of the current study

Beyond the investigation of the specificity of cognitive impairment in BN, the data gathered in this study will be incorporated into the Tayside Eating Disorder Research Group's ongoing research into the neuropsychological profile of eating disorders. Data from a group of healthy control participants was collected by the research group, administering the same neuropsychological measures used in the current study. Therefore, data from an additional healthy control group was not collected as part of the current study. The neuropsychological measures administered to participants, which were not a priori key measures of set shifting and inhibition, were included in the current study in order to facilitate comparison of this data with Research Group data already collected from AN groups and healthy controls.

3.4 Summary

As stated in the introduction, the aim of this thesis is to contribute to the body of research investigating the neuropsychological profile of bulimia by considering the specificity of the cognitive impairments reported in the literature. The potentially confounding influences of comorbid anxiety disorders and depression in BN have been highlighted in recent reviews as a neglected area of research (Van den Eynde *et al.*, 2011; Zakzanis *et al.*, 2010). Therefore, this study incorporates a comparison group of anxious and/or depressed outpatients.

Current eating disorder theory emphasises the similarity between eating disorders and supports research investigating the presence of similar properties in BN as have been seen in AN. It also proposes potential shared maintaining factors of severe perfectionism, low self esteem, mood intolerance and interpersonal difficulties. These potential maintaining factors of BN will also be explored by this thesis, particularly in the areas of self esteem and social problem solving.

3.4.1 Study Aims

1. To investigate what differences are evident, if any, between the a BN group and a comparison group of anxious and/or depressed adult females on measures of general psychopathology, eating pathology, set shifting and cognitive inhibition.
2. To investigate the relationships between general psychopathology, eating pathology, set shifting and inhibition within the groups.
3. To investigate social problem solving and self esteem in BN, and any relationship they may have to set shifting and cognitive inhibition

Chapter 4: Investigating the specificity of neuropsychological impairment in bulimic outpatients: a comparison with anxious and depressed outpatients.

Following guidelines of Journal of the International Neuropsychological Society (Appendix 5)

Abstract

Background: Bulimia Nervosa (BN) has been associated with deficits in set shifting and inhibition but reported results are inconsistent. Systematic reviews have highlighted the potentially confounding effects of comorbid disorders, and the specificity of deficits in BN has not been explicitly investigated

Method: Twenty one female participants with BN were compared to 23 females, in treatment for anxiety and/or depression, on neuropsychological measures of set shifting and inhibition, including the Wisconsin Card Sorting Test, the Trail Making Test and the Stroop task. Psychological symptoms were measured using the Symptom Checklist 90-R, the Yale Brown Obsessive Compulsive Scale and the Eating Disorder Examination.

Results: No group differences were found on a priori selected neuropsychological measures or measures of anxiety, depression or obsessive-compulsive symptoms. The BN group reported significantly more eating disorder symptoms than the comparison group.

Conclusions: These findings suggest that, in this sample, there is no evidence of a specific neuropsychological deficit in BN and suggest that deficits seen are shared with other disorders.

4.1 Introduction

Bulimia nervosa (BN) is characterised by binge eating accompanied by a sense of lack of control, the use of compensatory behaviours such as vomiting or excessive exercise, and self-evaluation unduly influenced by shape and weight (American Psychiatric Association, 2000). Both anorexia and bulimia involve rigid beliefs

about eating and purging, and strict adherence to personal rules, which have been associated with compulsive behaviour (Naylor et al., 2011). Compulsive behaviours are defined by Robbins et al. (2012) as “actions inappropriate to the situation which persist”, or as “a maladaptive perseveration of behaviour” (p83). Compulsive behaviour and the related construct of perfectionism are common in BN, and are associated with impaired neuropsychological task performance on measures of set-shifting (Egan et al., 2011; Tchanturia, Morris, et al., 2004). Impulsivity is also a feature of BN. This characteristic most commonly takes the form of bingeing behaviours, but BN is also associated with higher rates of shoplifting, substance abuse and self harm (Goldner et al., 2000; Hudson et al., 2007; Ruuska et al., 2005). A number of studies have linked impulsivity to cognitive disinhibition in BN patient groups and other disorders, suggesting a relationship between these variables (Kemps & Wilsdon, 2010; Kirisci et al., 2004; Rosval et al., 2006; Verdejo-García et al., 2006). Impulsive-compulsive behaviours often co-occur in BN and may be a reflection of underlying cognitive deficits in the areas of set-shifting and cognitive inhibition (Engel et al., 2005).

These neuropsychological deficits have become an area of interest for research as they are hypothesised to be the basis for some key symptoms of BN. Fairburn et al. (2003) theorise that clinical perfectionism, which is associated with compulsive behaviour and poor set shifting, is a key maintaining factor for some individuals with BN (Tchanturia et al., 2004). Where patients have a difficulty with set shifting, there can also be a difficulty engaging with CBT and using flexible thinking during the course of therapy. Current research in AN suggests that intervention directed at set shifting, where it is a difficulty, improves CBT treatment outcomes (Tchanturia et al., 2007). Observed impulsive bingeing and purging behaviour is theorised by Robinson et al. (2009) to relate to poor cognitive regulation of an underlying trait impulsivity. They propose that specific training in cognitive control to reduce impulsivity could be helpful to BN patients as part of therapy. Research demonstrating that lower impulsivity is associated with better treatment outcome supports this (Castellini et al., 2012).

The majority of neuropsychological research in eating disorders has focused on set-shifting ability in anorexia nervosa (AN), finding specific cognitive deficits as compared to healthy controls (HC) (Roberts et al., 2007). Comparisons have also been made between AN and other psychiatric groups such as obsessive compulsive disorder (OCD) (Murphy et al., 2004) and depression (Giel et al., In Press) to further clarify the specificity of these deficits. An increasing amount of research is now focussing on the neuropsychological profile of BN (Van den Eynde et al., 2011). As AN and BN are closely linked (Fairburn et al., 2003), set-shifting has also been a focus of research when investigating the neuropsychological profile of BN. While cognitive impairments have been reported in BN, there is little agreement between studies. Three recent systematic reviews on the topic have reached conflicting conclusions. Zakzanis et al. (2010) concluded that the core impairment in BN was an impairment in inhibition without impairments in set shifting, while the opposite trend was reported by Roberts et al. (2007). These reviews were limited in the number of studies they included, reviewing 14 and 4, respectively. The most recent comprehensive review examined 34 studies, reporting that the area was under-researched and that findings to date were inconclusive (Van den Eynde et al., 2011).

In Van den Eynde et al.'s (2011) review, impairment in inhibition was seen in BN in only one of five studies that used the classic Stroop task (Kemps & Wilsdon, 2010). Similarly, no clear pattern of impairment of inhibition was seen in studies using the Go/NoGo task or Matching Familiar Figures Test (Claes et al., 2006; Kemps & Wilsdon, 2010; Rosval et al., 2006; Southgate et al., 2008). One reviewed study used the Hayling sentence completion task as a measure of inhibition and found impairment in individuals with BN relative to controls (Kemps & Wilsdon, 2010). The Wisconsin Card Sorting Test (WCST) subscale of 'number of non-perseverative errors' has also been considered as a measure of inhibition. Alvarez-Moya et al. (2009) noted that individuals with BN had difficulty maintaining the correct set on the WCST, scoring significantly worse than controls on 'non-perseverative errors'. The WCST is usually used as a measure of set shifting ability, with 'number of perseverative errors' used as a key measure of compulsive responding behaviour. Bulimic patients have demonstrated impairment relative to HCs using this variable in

some studies, although an equal number of studies have found no significant differences (Alvarez-Moya et al., 2009; Brand et al., 2007). Similarly, set shifting as measured by the Trail Making Task (TMT) has produced mixed results (Roberts et al., 2010; Tchanturia, Anderluh, et al., 2004).

Cognitive impairment in inhibition and set shifting has been seen across a range of other disorders. Studies on neuropsychological deficits in anxiety disorders have reported set shifting and inhibition impairment in Post Traumatic Stress Disorder (PTSD) and Obsessive Compulsive disorder (OCD) (Kuelz et al., 2004; Polak et al., 2012), but not in social anxiety, simple phobia, panic disorder or generalised anxiety disorder (Airaksinen et al., 2005; O'Toole & Pedersen, 2011; Chapter 2 of this thesis). (Ferreri, *et al.*, 2011) Depression has also been associated with neuropsychological impairments in inhibition and set shifting (Gohier et al., 2009; Porter et al., 2007; Xu et al., 2012). However, much of the literature on depression has focused on the elderly, with deficits not consistently seen in young adult samples with mild to moderate depression (McClintock et al., 2010). When anxiety and depression co-occur, some research has reported increased impairments (Basso et al., 2007; Lyche et al., 2011), while others have reported that such clinical groups perform no differently to those with depression alone (Herrera-Guzman et al., 2009) or healthy controls (Graver & White, 2007). In anxiety and depression, as in BN, reviews indicate potential deficits in areas of set shifting and inhibition but conclude that further research and clarification of neuropsychological findings is required (Castaneda et al., 2008; Ferreri et al., 2011).

One possible confounder in assessments of neuropsychological performance is diagnostic comorbidity. Bulimia nervosa is frequently comorbid with both depression and anxiety disorders; up to 80% comorbidity is found with anxiety disorders and 60% comorbidity with Major Depressive Disorder (MDD) or dysthymia (Hudson et al., 2007). Overall, the neuropsychological literature in relation to BN is somewhat equivocal and the large clinical overlap with other disorder groups that also display similar cognitive impairments calls into question the specificity of the impairments seen in BN.

The reviews by both Van den Eynde et al. (2011) and Zakzanis et al. (2010) recommend that future research consider this overlap of diagnoses and symptoms when investigating the neuropsychological profile of BN. It is currently unclear if reported cognitive impairments are specific to BN or whether they are shared across other psychiatric diagnoses, representing a transdiagnostic, rather than disorder-specific feature. Knowledge about the specificity of cognitive impairments is important, in order to facilitate the development of disorder specific cognitive models and therapies (Dudley et al., 2011).

While one study has compared BN patients to OCD patients on neuropsychological measures (Murphy et al., 2004), no study to date has focused on further clarifying the specificity of reported cognitive impairments in BN through the use of a clinical group reflecting diagnoses that often co-occur with BN. The current study compared a group of females in psychological treatment for anxiety and/or depression (AD group), who were free from comorbid eating disorder, to a BN group. This study sought to investigate what differences, if any, exist between the two groups on measures of set shifting and inhibition. Further exploratory analyses were conducted on the relationships between reported anxiety, depression, obsessive compulsive and eating disorder symptoms and performance on the neuropsychological measures.

4.2 Methods

4.2.1 Participants

The BN group consisted of 21 outpatients, 14 with BN and 7 with Eating Disorder Not Otherwise Specified-Bulimic Type (EDNOS-BN), recruited from eating disorder services of NHS Grampian (n=5) and NHS Tayside (n=16). All patients meeting inclusion criteria and in treatment for BN with the NHS Tayside (29) were provided with study information by their clinicians. Patients in Grampian meeting the inclusion criteria were posted study information by their clinician. The number of patients contacted in Grampian was not available at the time of writing. Patients with EDNOS were included if they had subthreshold bulimic symptoms and were therefore being treated as a bulimic patient as per National Institute for Health and Clinical Excellence (NICE) guidelines for the treatment of EDNOS (NICE, 2004a). EDNOS patients with primarily anorexic features and patients with Binge Eating Disorder were excluded. Participants in the AD group were 23 outpatients in treatment for major depressive disorder (MDD) and/or an anxiety disorder in the Tayside Adult Psychological Therapies Service. A breakdown of their diagnoses appears in Table 4.1. AD group participants were required to score 11 or more on either scale of the Hospital Anxiety and Depression Scale (HADS: Zigmond & Snaith, 1983). All participants were adult females recruited between November 2011 and June 2012. All diagnoses met Diagnostic and Statistical Manual, 4th edition (DSM-IV; American Psychiatric Association, 2000) criteria, as determined by the treating clinician.

Table 4.1 Diagnoses of AD group

Diagnosis	Number of participants
Anxiety	11
GAD	3
PD (with agoraphobia)	3
Agoraphobia	1
Specific Phobia	1
OCD	2
Health Anxiety	1
MDD	3
Mixed anxiety and depression	9

MDD = Major Depressive Disorder, GAD = Generalised Anxiety Disorder,
PD = Panic Disorder

Patients were excluded if they were medically unstable, had a history of learning disability, substance abuse, developmental or neurological disorder, an uncorrected visual or motor impairment, or previous head injury involving loss of consciousness. In addition, AD group participants were excluded if they demonstrated significantly disordered eating (Eating Disorder Examination score ≥ 4). The study was approved by NHS Tayside Research Ethics Committee and all participants gave written informed consent.

The groups were matched on years of education, estimated premorbid IQ and Body Mass Index (BMI) (see Table 4.2). However, bulimic patients were significantly younger than AD group patients ($t(42) = 2.918$; $p < .008$). Mean age of disorder onset was also significantly lower in the BN group than in the AD group ($U = 129$, $Z = -2.65$, $p < .008$). Ninety percent of the BN group were right-handed compared to 74% of the AD group. This difference was not found to be significant using Fisher's exact test ($p = .432$). Two BN participants reported having a previous diagnosis of anorexia. Forty eight percent of the BN participants and 65% of the AD participants were taking psychiatric medication, primarily antidepressants (5 SSRI, 3 serotonin-norepinephrine uptake inhibitors (SNRI) and 1 tetracyclic antidepressant in the BN group, 9 SSRI and 3 tetracyclic antidepressants in the AD group). Two BN participants were taking Quetiapine, while in the AD group one person was taking

Diazepam and one was taking Tramadol. No medications had been changed within the previous month.

Table 4.2: Characteristics of groups

	BN group n=21			AD group n=23			Cohen's				
	<i>Mean</i>	<i>SD</i>	<i>Median (range)</i>	<i>Mean</i>	<i>SD</i>	<i>Median (range)</i>	<i>t</i>	<i>U</i>	<i>p</i>	<i>d</i>	<i>r</i>
Clinical Characteristics											
Age (yrs)	29.29	10.49		39.52	12.75		2.918		.006**	-0.89	
Education (yrs)	14.60	2.41		15.17	2.91		0.721		.475	-0.22	
BMI (Kg/m ²) ^a	24.07	4.15	24.5 (17.4-32.4)	26.96	6.90	24.5 (18.5-45.6)		178.5	.319		-0.16
Age of disorder onset	18.19	7.28	16 (7-38)	29.43	14.87	27 (11-62)		129	.007**		-0.40
Duration of disorder	10.17	7.45	9 (1-32)	9.19	11.85	3 (0.04-38)		170	.047*		-0.25
NART estimated FSIQ	110.61	5.97		111.39	5.40		0.451		.665	-0.14	

Note. BMI= Body Mass Index, BN=Bulimia Nervosa, AD= Anxiety and/or Depression

* $p < 0.05$

**Bonferroni correction for 6 comparisons $\alpha=.008$

a: data available for only 42 patients (data missing for 2 BN participants)

4.2.2 Measures

Participants were administered a battery of standardised assessment measures relating to psychopathology and neuropsychological performance in the areas of set shifting and cognitive inhibition.

4.2.2.1 Psychopathology Measures

Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983)

The HADS is a self-report measure containing two scales relating to anxiety and depression symptoms. The HADS depression subscale has 90% sensitivity and 86% specificity for depression compared to the gold standard of a structured diagnostic interview (Zigmond & Snaith, 1983). Good reliability for both scales has been well documented in adults. A recent review by Bjelland *et al.* (2002) reported the reliability of the Anxiety subscale to vary from 0.68 to 0.93 (mean 0.83) and for the Depression subscale from 0.67 to 0.90 (mean 0.82). The HADS was administered to AD group patients as part of routine clinical practice. A score of 11 or more on either scale indicated moderate to severe symptoms.

Eating Disorders Examination (EDE) Version 12 (Fairburn & Cooper, 1993)

The EDE is a semi-structured clinical interview, which measures eating disordered attitudes and behaviours. It contains four subscales (Dietary Restraint, Eating Concern, Weight Concern and Shape Concern), and a global score. All subscale mean scores and the global score range from 0-6. Good internal consistency, (Beumont *et al.*, 1993; Cooper *et al.*, 1989) concurrent (Rosen *et al.*, 1990) and discriminant (Cooper *et al.*, 1989; Rosen *et al.*, 1990; Wilson & Smith, 1989) validity, and inter-rater reliability (Black & Wilson, 1996; Cooper & Fairburn, 1987; Rosen *et al.*, 1990; Wilson & Smith, 1989) have been demonstrated for the EDE in adults.

Yale–Brown Obsessive Compulsive Scale–Symptom Check List (Y–BOCS–SC) (Goodman, Price, Rasmussen, & Mazure, 1989)

The YBOCS consists of a 58 item symptom checklist and a 10 item severity scale. The symptom checklist covers a range of obsessions and compulsions, clustered by behavioural expression and thematic content. Obsessions and compulsions are assessed over the 5 dimensions of time spent, interference in functioning, distress, efforts to resist and perceived control, creating a 10 item severity measure relating to the past 7 days. The YBOCS can be administered in the form of interview or self-report. Good agreement has been found between these for both the symptom checklist and severity ratings (Steketee et al., 1995). The current study used a self-report version (Baer, 1991).

Symptom Check List-90 Revised (SCL-90-R) (Derogatis, 1994; Derogatis et al., 1973)

The SCL-90-R is a 90-item self-report instrument for measuring general psychopathology for use with community, medical and psychiatric respondents. It comprises nine primary symptom dimensions; - Somatisation, Obsession-Compulsion, Interpersonal Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation and Psychoticism - and three global indices; the Global Severity Index (GSI), the Positive Syndrome Distress Index (PSDI) and the Positive Symptom Total (PST). Good internal consistency of the primary symptom dimensions and global indices has been demonstrated across a number of populations. The SCL-90-R has been found to have good test-retest reliability across a range of patient groups and test-retest intervals (Derogatis, 2000). The Depression and Anxiety subscales have the most evidence of convergent and discriminant validity (Bech et al., 1992; Derogatis, 2000; Koeter, 1992). The Obsession-Compulsion subscale has been shown to be internally consistent (Woody et al., 1995) but also demonstrates poor discriminant validity, therefore the YBOCS was taken as the primary measure of obsessive compulsive symptoms in this study (Kim et al., 1992; Woody et al., 1995).

4.2.2.2 Neuropsychological Measures

National Adult Reading Test (NART) (Nelson, 1982; Nelson & Willison, 1991)

The NART is a measure of premorbid intellectual ability. The participant is asked to read aloud 50 irregularly spelled words (e.g. cough). The number of pronunciation errors is used to estimate the Wechsler Adult Intelligence Scale-Revised (WAIS-R; Wechsler, 1981) full scale IQ from standardised norms. The NART's validity as a measure of premorbid intelligence has been well documented (e.g. Crawford et al., 2001).

Delis–Kaplan Executive Function System (D-KEFS) (Delis et al., 2001)

Two tests from the D-KEFS were used:

Colour Word Inference Test (CWIT) – This is a measure of response inhibition and cognitive flexibility based on the Stroop procedure. The CWIT has four conditions: colour naming (condition 1), word reading (condition 2), inhibition (colour word interference, condition 3) and set shifting (Inhibition Switch, condition 4). In each condition, the outcome is the time taken to read 50 items and the number of errors made.

Trail Making Test (TMT) – This is a measure of planning and cognitive flexibility based on the traditional TMT A and B. The TMT has 5 conditions: visual scanning (condition 1), number sequencing (condition 2), letter sequencing (condition 3), number-letter switching (condition 4), and motor speed (condition 5). The procedure for the first condition involves a timed visual search. The remaining conditions involve drawing a line connecting the target items (numbers, letters or empty circles) as quickly as possible. The switching task involves switching back and forth between connecting numbers and letters, completing the task as quickly as possible. In each condition, the outcome measures are time to complete task and number of errors. Good to moderate test retest reliability and internal consistency are described in the technical manual for CWIT and TMT (Delis et al., 2001).

The Hayling task (Burgess & Shallice, 1997)

The Hayling task evaluates initiation speed, by requiring participants to complete 15 sentences as quickly as possible. Part one requires sensible completion of the sentence while part two requires an unrelated word. This is a measure of response suppression. Outcome measures are the time taken to respond and total number of errors. Adequate inter-rater reliability and test-retest reliabilities have been reported for this task (Andres & Van der Linden, 2000; Burgess & Shallice, 1997).

Wisconsin Card Sort Test (WCST) (Heaton et al., 1993)

The WCST measures concept formation, set-shifting, and set maintenance. Four stimulus ‘key cards’ with symbols differing in colour, shape and number are placed in front of the participant, who is given a pack of 128 response cards and instructed to match each response card to one of the key cards. The researcher only provides feedback of ‘correct’ or ‘incorrect’ for each trial. After coupling 10 cards with the first criterion (colour), the subject is required to shift to the second criterion (shape) and then to the third (number). The procedure is repeated twice or until all 128 cards have been used. Good test-retest and inter-rater reliabilities have been reported in adults (Axelrod et al., 1992; Bowden et al., 1998; Heaton et al., 1993). The official computer package was used to score this task.

4.2.3 Measures selected as a priori key variables for set shifting and inhibition

Seven specific variables were selected from the neuropsychological battery as a priori key measures. The key variables chosen were those on which neuropsychological deficits have been previously reported in BN patients compared to HCs. The 4 key variables selected to reflect set shifting performance were ‘number of perseverative errors’ and ‘categories completed’ from the WCST (Roberts et al., 2010) and the completion time and number of errors in TMT condition 4 (Brand et al., 2007; Konstantakopoulos et al., 2011; Roberts et al., 2010; Tchanturia, Morris, et al., 2004). The 3 key variables selected to reflect cognitive inhibition were the WCST ‘number of non-perseverative errors’ (Alvarez-Moya et al., 2009), condition 3 from the CWIT and the number of errors made on the Hayling

task part two (Kemps & Wilsdon, 2010). Information on the additional outcome variables included in the above measures was provided in the form of secondary variables, as recommended by Van den Eynde et al.'s (2011) review.

4.2.4 Procedure/Protocol

Suitable patients were identified by their clinician and invited to participate. They were provided with study information and contacted by the first author no sooner than 24 hours after expressing interest in the study. Demographic and historical information relating to participant characteristics was collected first using a questionnaire designed for the study, followed by administration of the EDE, the neuropsychological battery (in the order listed above) and the self report measures (in the order listed above). Testing lasted approximately 1.5 to 2 hours.

4.2.5 Data Analysis

Data were analyzed using SPSS (version 15). Means were calculated for all continuous variables and frequencies for categorical variables. Means of the two groups were compared on assessment measures and demographic characteristics using t-tests, where data were normally distributed. The non-parametric Mann Whitney U statistic was used to compare non-normal variables between groups. Appropriate effect sizes, Cohen's d or r , were calculated for these comparisons. Associations between a priori key measures and psychopathological variables within groups were investigated using the non-parametric Kendall's tau.

4.2.5.1 Power for comparison of means

The literature indicated expected effect sizes ranging from 0.78 to 1.2 for differences between BN and AD groups. This suggested optimal samples sizes of 26 in order to detect large effect sizes ($d=0.8$, $r=0.5$) using the parameters of a power of 80% and a 0.05 two tailed significance level. Due to difficulties with recruiting this number of participants, the resulting sample sizes had the power to detect an effect size of $d=0.88$ with a power of 80% and a 0.05 two tailed significance level (calculated using GPower 3.1.2).

4.3 Results

4.3.1 Group comparisons on psychological and neuropsychological measures

Participants on medication did not perform significantly differently on key measures to those not taking medication using Mann Whitney U tests (all $p > .05$). Descriptives and statistical group comparisons for psychological and neuropsychological variables are presented in Table 4.3 and Table 4.4 respectively.

The BN group was not significantly different to the AD group in self reported obsessive compulsive symptoms as measured by the YBOCS, or on any of the symptom clusters measured by the SCL-90-R including anxiety and depression. The BN group scored significantly higher than the AD group on all scales of the EDE.

On the a priori measures of set shifting and inhibition, the BN group did not perform significantly differently from the AD group (See Table 4.4). As groups differed significantly on age, differences between the groups on age normed scaled scores were investigated on neuropsychological measures where such scaled scores were available. There were also no significant differences using age normed scores (all $p > .05$).

Table 4.3: Comparison of groups on psychological variables

	Bulimic group n=21			Anx/Depressed group n=23			Cohen's				
	<i>Mean</i>	<i>SD</i>	<i>Median (range)</i>	<i>Mean</i>	<i>SD</i>	<i>Median (range)</i>	<i>t</i>	<i>U</i>	<i>p</i>	<i>d</i>	<i>r</i>
Psychological Measures											
SCL-90 (GSI)	1.37	0.68		1.16	0.58		1.14		.262	0.34	
O-C	18.00	8.80		13.26	6.57		2.04		.048	0.61	
Depression	25.33	10.95		22.39	11.70		0.86		.395	0.26	
Anxiety	11.33	8.41	9 (1-35)	12.57	8.61	14 (0-34)		216.5	.564		-0.09
Phobia	5.38	6.47	2.5 (0-21)	7.83	6.80	7 (0-22)		185.0	.185		-0.20
Somatisation	14.91	10.87	12.5 (1-41)	9.52	7.51	7 (0-23)		170.0	.094		-0.25
Hostility	5.19	3.37		4.22	3.36		0.96		.343	0.28	
I-S	16.62	6.45		12.78	8.08		1.73		.091	0.53	
YBOCS^a	13.75	7.35	14.5 (0-27)	9.96	7.96	9 (0-24)		159.0	.084		-0.27
EDE											
Restraint	3.60	1.38	3.8 (0.3-6)	1.04	1.19	1.1(0.08-3.14)		42.5	.001*		-0.71
Eating concern	3.21	1.36	3.3 (0.6-5.2)	0.41	0.64	0 (0-2.2)		15.5	.001*		-0.81
Shape concern	4.59	1.04		1.61	0.92		10.11		.001*	3.04	
Weight concern	4.10	1.22	4.1 (1.4-6)	1.37	1.17	0.8 (0-3.6)		29.5	.001*		-0.75
Global Score	3.87	1.00		1.11	0.74		10.46		.001*	3.14	

Note. SCL-90= Symptom Checklist-90-Revised, GSI= Global Severity Index, O-C = obsessive-compulsive scale, I-S = interpersonal sensitivity, YBOCS= Yale-Brown Obsessive Compulsive Scale, EDE= Eating Disorder Examination (Version 12), Anx=Anxious. all analysis are two tailed, $r = Z/\sqrt{N}$

a: n=20 in BN group

* indicates significance at Bonferroni corrected alpha level of 0.05/17=.002

Table 4.4: Comparison of groups on key Set Shifting and inhibition variables

Set Shifting	Bulimic group n=21			Anxious/Depressed group n=23			<i>t</i>	<i>U</i>	<i>p</i>	Cohen's	
	<i>Mean</i>	<i>SD</i>	<i>Median (range)</i>	<i>Mean</i>	<i>SD</i>	<i>Median (range)</i>				<i>d</i>	<i>r</i>
WCST											
Perseverative errors	10.71	6.37	10 (4-28)	14.04	11.96	8 (4-52)		211.5	.487		-0.11
Categories completed	5.19	1.66	6 (0-6)	4.91	1.83	6 (0-6)		217.0	.481		-0.11
DKEFS											
Trail Making test			73.2 (20.1-			71.1 (41.5-					
Number/letter switch	69.21	22.41	120.9)	76.12	26.31	161.4)		228.0	.758		-0.05
Trail Making test No. of errors	0.91	1.95	0 (0-8)	0.35	0.94	0 (0-4)		210.5	.331		-0.15
Inhibition											
WCST											
Non-perseverative errors	16.62	20.46	7 (2-74)	13.91	11.72	9 (3-41)		241.0	.995		-0.001
DKEFS											
Colour Word Inhibition	47.06	10.67	46.1 (30.8-67.5)	52.05	14.31	49.4 (28.4-91.7)	1.30		.200	0.19	
Hayling Errors	1.05	1.99	1 (0-7)	2.35	4.10	1 (0-18)		193.0	.235		-0.18
Secondary Measures											
WCST											
Number of trials to complete first	16.76	25.73	11 (10-129)	18.30	25.06	11 (10-129)		224	.654		-0.069
% Conceptual level responses	68.05	23.54	76 (9-91)	67.35	21.57	77 (13-90)		223	.670		-0.066
Failure to maintain set	0.43	0.60	0 (0-2)	0.91	1.56	0 (0-7)		206.5	.354		-0.140
Learning to learn			-1.26 (-32.6-3.9)			-1.04 (-28.59-		219.5			-0.004
	-3.68	8.54		-2.52	6.82	7.32)			.985		
Trials administered	95.57	22.17	92 (70-128)	97.91	24.67	85 (70-128)		232.5	.836		-0.032
Colour Word			51.1 (33.7-74.1)			61.9 (41.7-91.2)					
Inhibition Shift	52.82	12.94		64.56	15.06		2.76		.009*	-0.84	

* $p < .01$, **indicates significance at Bonferroni corrected alpha level of $0.05/7=.007$ for à priori key variables,

† indicates significance at Bonferroni corrected alpha level of $0.05/10=.005$ for secondary variables, all analysis are two tailed, $r = Z/\sqrt{N}$

4.3.2 Relationship of Psychopathological Symptoms to Set Shifting and inhibition

Relationships between neuropsychological performance and anxiety or depression symptoms, as measured by the SCL-90-R or obsessive compulsive symptoms as measured by the YBOCS were investigated using Kendall's tau correlations within each group. Correlations were performed between the seven a priori key variables, the three psychopathological measures and the subscales of the EDE (Table 4.5).

A significance level of $p < .01$ was chosen, as a Bonferroni correction was considered too conservative for this analysis. There was a significant relationship between the number of Hayling task errors and EDE Eating Concern in the BN group. Within the AD group, the YBOCS correlated with WCST categories completed (0.46) and anxiety was correlated with TMT errors (-0.48) (Table 4.6). However, there were strong floor effects on the Hayling task and TMT errors and a ceiling effect in the WCST categories completed. On visual inspection of the variables, within the AD group, the YBOCS correlation did not appear to be a true relationship (graphs in Appendix 6).

Table 4.5: Correlation of Set shifting and inhibition key measures with psychopathology measures in bulimic group

	SCL-90		YBOCS		EDE		
	<i>Anx</i>	<i>Dep</i>		<i>Restraint</i>	<i>Eating</i>	<i>Shape</i>	<i>Weight</i>
<u>Set Shifting</u>							
WCST							
Perseverative errors	.045	.130	.126	-.130	.069	-.177	-.104
Categories completed	.164	-.104	-.040	-.089	-.118	-.022	-.059
DKEFS							
Trail Making test							
Number/letter switch	-.087	-.044	.133	-.277	-.043	-.053	-.329*
Trail Making test							
Number of errors	-.007	-.070	.225	.042	.213	-.110	-.166
<u>Inhibition</u>							
WCST							
Non-perseverative errors	.044	.118	.141	.020	.214	.019	.005
DKEFS							
Colour Word							
Inhibition	.189	-.058	.149	-.194	.010	.029	-.149
Hayling							
Errors	-.247	-.400*	-.006	-.406*	-.522**	-.052	-.222

Note. SCL-90= Symptom Checklist-90-Revised, YBOCS= Yale-Brown Obsessive Compulsive Scale, EDE= Eating Disorder Examination (Version 12). *Anx* = Anxiety subscale, *Dep* = Depression subscale, * $p < .05$, ** $p < .01$,

Table 4.6 Correlation of key set shifting and inhibition measures with psychopathology in the AD group

	SCL-90		YBOCS		EDE		
	<i>Anx</i>	<i>Dep</i>		<i>Restraint</i>	<i>Eating</i>	<i>Shape</i>	<i>Weight</i>
WCST							
Perseverative errors	-.016	.045	-.230	-.174	-.024	.045	-.168
Categories completed	.127	.058	.462**	.241	.232	.090	.242
Non-perseverative errors	-.012	.127	-.382*	-.287	-.114	-.012	-.257
DKEFS							
Trail Making test							
Number/letter switch	-.177	-.044	-.216	.122	-.009	.004	-.016
Trail Making test							
Number of errors	-.484**	-.345*	-.014	.385*	-.229	-.263	.036
Colour Word							
Inhibition	-.121	-.171	-.061	.017	-.148	-.012	-.090
Hayling							
Errors	-.072	-.080	.082	.054	-.104	-.040	-.151

Note. SCL-90= Symptom Checklist-90-Revised, YBOCS= Yale-Brown Obsessive Compulsive Scale, EDE= Eating Disorder Examination (Version 12), *Anx* = Anxiety subscale, *Dep* = Depression subscale * $p < .05$, ** $p < .01$,

4.3.3 Post hoc exploratory analysis

4.3.3.1 Association between psychopathological variables and neuropsychological performance using data from combined groups

As no significant differences were found between groups on the a priori neuropsychological measures, the two groups were combined and Kendall's tau correlations were used to investigate associations between psychopathological variables and neuropsychological performance in the entire sample (Table 4.7). Using the whole sample, significant correlations ($p < .05$) were seen between the YBOCS and WCST categories completed (0.25), and between SCL-90-R Anxiety and TMT errors (-.25). For the same reasons as above, these relationships must be interpreted with caution due to the noted floor and ceiling effects. Again, the YBOCS correlation did not appear to be a true relationship. Graphs are provided in Appendix 6.

Table 4.7: Correlation of key set shifting and inhibition measures with psychopathology in both groups combined

	SCL-90		YBOCS
	<i>Anx</i>	<i>Dep</i>	
WCST			
Perseverative errors	.030	.075	-.100
Categories completed	.100	.002	.253*
Non-perseverative errors	.020	.126	-.120
DKEFS			
Trail Making test			
Number/letter switch	-.176	-.103	-.036
Trail Making test			
Number of errors	-.247*	-.170	.116
Colour Word			
Inhibition	.001	-.132	-.006
Hayling			
Errors	-.134	-.211	.007

Note. SCL-90= Symptom Checklist-90-Revised, YBOCS= Yale-Brown Obsessive Compulsive Scale, Anx = Anxiety subscale, Dep = Depression subscale
 $*p < .05$, $**p < .001$,

4.3.3.2 Regression

Further analysis explored any possible predictive relationship between anxiety, depression and obsessive symptoms and neuropsychological performance, using multiple linear regression analysis. A priori key variables were used as the dependent variables and the YBOCS and the SCL-90-R subscales of anxiety and depression were independent variables (Table 4.8). Seven separate linear regression analyses were performed.

Using 43 participants (one participant did not complete the YBOCS) this sample had the power to detect a large effect size using 3 predictors (power 0.8, $\alpha = .5$) according to the calculations of Miles and Shevlin (2001). Due to the non-normality of the data, some outliers were removed for regression analysis (detailed in Table 4.8). In order to control for interaction effects between predictors, all variables entered the regression analysis simultaneously. Relationships between variables were investigated using Kendall's tau correlations and examination of eigenvalues. The anxiety and depression subscales of the SCL-90-R were noted to correlate and to load primarily on the same small eigenvalue, indicating some collinearity. No bivariate correlations exceeded 0.70 so no variables were excluded (Tabachnick & Fidell, 2001). The assumption of normally distributed errors of the regression was violated for a number of the models, as determined from examination of graphs and a Kolmogorov-Smirnov test on the standardised residuals. This violation of assumptions suggests that the results of the regression analysis will generalise poorly.

None of the models were significant (for all F values, $p > .05$), suggesting that in this sample, anxiety, depression and obsessive compulsive symptoms did not predict neuropsychological performance.

Table 4.8: Adjusted Beta values for predictor variables in the regression analyses

	WCST			TMT		CWIT	Hayling
	Perseverative errors ^a	Categories completed ^{bh}	Non perseverative errors ^c	Number/letter switch ^d	Number of errors ^{eh}	Inhibition ^f	Errors ^{gh}
	Beta	Beta	Beta	Beta	Beta	Beta	Beta
SCL-90							
Anxiety	-0.06	-0.154	-0.09	-0.311	-0.426	0.128	-0.222
Depression	0.32	-0.091	0.197	-0.07	0.035	-0.356	-0.526*
YBOCS	-0.317	0.283	-0.343*	-0.018	0.254	-0.025	0.002
AdjR ²	0.086	0.021	-0.024	0.070	0.088	0.009	0.106
F	2.283	1.295	0.666	2.046	2.315	1.124	2.615

* $p < .05$, ** $p < .01$, *** $p < .001$

a $n=42$, 1 outlier removed, 4 standard deviations from the mean

b $n=43$ because data is missing for one BN participant on YBOCS

c $n=41$, 2 outliers removed, each 3.2 standard deviations from the mean

d $n=43$,

e $n=42$, 1 outlier removed, 4.62 standard deviations from the mean

f $n=42$, 1 outlier removed, 3.2 standard deviations from the mean

g $n=42$, 1 outlier removed, 4.76 standard deviations from the mean

h assumption of normality of errors violated

4.3.4 Exploratory analysis of performance on secondary set shifting and inhibition variables

4.3.4.1 Analysis of Secondary Variables

The BN group were significantly slower on the CWIT condition 4 than the AD group with a large effect size of 0.84. However, this was no longer significant after Bonferroni correction (Table 4.4).

4.4 Discussion

The present study was the first to use a clinical comparison group of people with anxiety and/or depression to investigate the specificity of neuropsychological impairments among patients with BN. The a priori set shifting and inhibition variables were selected because they have been highlighted in the literature as demonstrating potential deficits in individuals with BN as compared to healthy controls (Alvarez-Moya et al., 2009; Brand et al., 2007; Roberts et al., 2010). No statistically significant differences were found between the BN group and the AD group on these measures, indicating similar levels of neuropsychological ability in both groups. While there was a significant relationship between anxiety and one neuropsychological measure, a regression analysis demonstrated that anxiety, depression and obsessive compulsive symptoms were not predictive of neuropsychological performance.

Although no studies were found that conducted neuropsychological comparisons between a BN and AD group, over half of the AD group were diagnosed with depression and literature would suggest that a depressed group may perform worse on tasks of inhibition and set shifting than an eating disordered group. Giel et al. (In Press) found that individuals with unipolar depression performed significantly worse than those with AN on set shifting, using the TMT and WCST perseverative errors, and on cognitive inhibition using the Parametric Go/NoGo task (PGNG; Langenecker et al., 2007). As the performance of BN patients in the literature is reported as the same or better than AN patients (Lauer et al., 1999; Roberts et al., 2010), it may have been expected that the BN group would also perform better than a depressed group. However, in Giel et al.'s (In Press) study, only AN patients without comorbid depression were included, and as a result, the AN group reported significantly fewer depression symptoms than the unipolar depression group. This was not the case in the current study where comorbid depression was not excluded in the BN group and similar levels of depression were reported in both groups. It is possible that an AN group with no comorbid depression is a particular subgroup of AN, which is not comparable to the BN sample of mixed comorbidity used in the current study. Subgroups of AN have been demonstrated to show significantly

different levels of ability on neuropsychological tasks (Lauer et al., 1999; Roberts et al., 2010).

The literature provides some indications that particular anxiety disorders, such as OCD and PTSD, may demonstrate greater impairment on inhibition and set shifting tasks than BN. Murphy et al. (2004) reported that BN participants performed significantly better on the TMT than an OCD group. However, while OCD is an anxiety disorder with replicated neuropsychological impairments (Martinez-Gonzalez & Piqueras-Rodriguez, 2008) most participants in the AD group were diagnosed with GAD, specific phobia or panic disorder with or without comorbid depression. The literature would suggest that these anxiety disorders are less likely to have specific deficits in set shifting or inhibition than a group of OCD patients, and are therefore less likely to differ from a BN group (Airaksinen et al., 2005; Chapter 2 of this thesis; McClintock et al., 2010; O'Toole & Pedersen, 2011).

In the BN group, higher scores on the EDE eating concern scale were significantly associated with fewer errors on the Hayling task, suggesting that those higher in Eating Concern were better able to inhibit incorrect responses on this task. However, this correlation was influenced by a floor effect and needs to be interpreted with caution. Within the literature for BN, eating disordered symptoms have not been found to be associated with neuropsychological performance, on set shifting measures such as the TMT (Murphy et al., 2004) on a task of conditional associative learning (Murphy et al., 2004) or on a gambling task (Guillaume et al., 2010). The finding, in this study, that most other neuropsychological measures were not correlated with ED symptoms is consistent with this literature.

No associations were found between anxiety, depression and obsessive-compulsive symptoms and neuropsychological performance in the BN group, consistent with the existing literature in BN, which has found no such associations using a cognitive flexibility test battery (Tchanturia, Anderluh, et al., 2004), the TMT (Murphy et al., 2004), and a decision making task (Brand et al., 2007). In the AD group and the combined groups, correlational analyses suggested some relationships between anxiety and TMT errors, and obsessive-compulsive symptoms and the WCST 'categories completed' variable. However, these relationships need to be interpreted

with caution due to the noted floor and ceiling effects. These correlations are not consistent with reports in the literature that psychological distress and trait anxiety are unrelated to TMT performance in young adults suffering from anxiety disorders (Castaneda et al., 2011). However, it should be noted that no significant associations were found on measures with more normally distributed data.

A regression model using anxiety, depression and obsessive-compulsive symptoms, did not predict performance on any a priori measure when data from the two groups were combined. This is consistent with the literature mentioned above, which has found no relationships between psychological symptoms and neuropsychological test performance in BN and anxiety groups. In relation to patients with depression, McClintock et al.'s (2010) review reported that associations between neuropsychological performance and depression symptoms have been found but are not consistent across studies.

4.4.1 Limitations

There are limitations to the present study, which may restrict the generalisability of the findings. The BN and AD groups in the current study were chosen on the basis of their primary diagnosis with no exclusion of comorbid major depression or anxiety disorder. The BN group were a general clinical group, with participants who potentially had comorbid anxiety disorders and/or major depression, as is common in BN (Hudson et al., 2007). However, there was no assessment of the BN participants for comorbid disorder. Such assessment could have further contributed to the understanding of the data.

The power achieved within the study due to sample size, meant that only effect sizes above $d=0.88$ were detectable as significant in group comparisons. A number of trends were observed in the data, which may have been found to be significant if the study had the statistical power to detect smaller effect sizes. However, Bezeau and Graves (2001) concluded that clinical neuropsychology research commonly deals with large effect sizes, suggesting that power to detect large effect sizes ($d=0.8$) is adequate.

4.4.2 Implications and future directions

The pattern of findings suggests that neuropsychological performance in BN is broadly the same as a clinical comparison group of anxious and/or depressed outpatients. This implies that deficits seen in studies comparing BN to HC may reflect impairments that are shared with other disorders, rather than impairments that are specific to BN. Future research may wish to document the comorbidities present in the BN sample or if possible include a BN group without comorbidities. The inclusion of comparison groups for anxiety disorders and major depression separately, might help to further clarify how cognitive impairments may be shared among common psychological disorders, whether there are causal effects of particular comorbid disorders or if the neuropsychological performance patterns are epiphenomena of pathology. The inclusion of a healthy control group would also be useful to examine how performance of clinical groups deviates from healthy performance. At present, these findings suggest that the development of therapies based on a specific neuropsychological profile of BN is unnecessary.

4.4.3 Conclusion

This study examined set-shifting and cognitive inhibition performance in 21 bulimic patients and 23 matched clinical comparison patients in treatment for anxiety and/or depression. The results indicated no significant differences between the two groups on a battery of neuropsychological tests focused on measures of set shifting and inhibition. Further analysis indicated that shared anxiety, depression and obsessive-compulsive symptoms were not predictive of neuropsychological test performance. These findings do not support the specificity of impairments in set shifting and inhibition in BN.

4.5 References

- Airaksinen, E., Larsson, M., & Forsell, Y. (2005). Neuropsychological functions in anxiety disorders in population-based samples: evidence of episodic memory dysfunction. *Journal of Psychiatric Research*, 39(2), 207-214.
- Alvarez-Moya, E.M., Jiménez-Murcia, S., Moragas, L., Gómez-Peña, M., Aymamí, M.N., Ochoa, C., Sánchez-Díaz, I., Menchón, J.M., & Fernández-Aranda, F. (2009). Executive functioning among female pathological gambling and bulimia nervosa patients: preliminary findings. *Journal Of The International Neuropsychological Society: JINS*, 15(2), 302-306.
- American Psychiatric Association. (2000). *Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-TR, 4th Edition, Text Revision*. Washington, DC: American Psychiatric Press, Inc.
- Andres, P., & Van der Linden, M. (2000). Age-related differences in supervisory attentional system functions. *Journal of Gerontology: Psychological Sciences*, 55, 373-380.
- Axelrod, B., Goldman, R., & Woodard, J. (1992). Interrater reliability in scoring the Wisconsin card sorting test. *The Clinical Neuropsychologist*, 6(2), 143.
- Baer, L. (1991). *Getting Control: Overcoming your Obsessions and Compulsions*. London: Plume Publishing.
- Basso, M.R., Lowery, N., Ghormley, C., Combs, D., Purdie, R., Neel, J., Davis, M., & Bornstein, R. (2007). Comorbid anxiety corresponds with neuropsychological dysfunction in unipolar depression. *Cognitive Neuropsychiatry*, 12(5), 437-456.
- Bech, P., Allerup, P., Maier, W., Albus, M., Lavori, P., & Ayuso, J.L. (1992). The Hamilton scales and the Hopkins Symptom Checklist (SCL-90). A cross-national validity study in patients with panic disorders. *The British Journal of Psychiatry*, 160(2), 206-211.
- Bezeau, S., & Graves, R. (2001). Statistical power and effect sizes of clinical neuropsychology research. *Journal of Clinical and Experimental Neuropsychology*, 23(3), 399-406.
- Bowden, S.C., Fowler, K.S., Bell, R.C., Whelan, G., Clifford, C.C., Ritter, A.J., & Long, C.M. (1998). The Reliability and Internal Validity of the Wisconsin Card Sorting Test. *Neuropsychological Rehabilitation*, 8(3), 243-254.
- Brand, M., Franke-Sievert, C., Jacoby, G.E., Markowitsch, H.J., & Tuschen-Caffier, B. (2007). Neuropsychological correlates of decision making in patients with bulimia nervosa. *Neuropsychology*, 21(6), 742-750.
- Burgess, P.W., & Shallice, T. (1997). *The Hayling and Brixton Tests*. Suffolk: Thames Valley Test Company.
- Castaneda, A.E., Suvisaari, J., Marttunen, M., Perala, J., Saarni, S.I., Aalto-Setälä, T., Lonnqvist, J., & Tuulio-Henriksson, A. (2011). Cognitive functioning in a population-based sample of young adults with anxiety disorders. 26(6), 346-353.
- Castaneda, A.E., Tuulio-Henriksson, A., Marttunen, M., Suvisaari, J., & Lonnqvist, J. (2008). A review on cognitive impairments in depressive and anxiety disorders with a focus on young adults. *Journal of Affective Disorders*, 106(1-2), 1-27.
- Castellini, G., Mannucci, E., Lo Sauro, C., Benni, L., Lazzeretti, L., Ravaldi, C., Rotella, C.M., Faravelli, C., & Ricca, V. (2012). Different Moderators of

- Cognitive-Behavioral Therapy on Subjective and Objective Binge Eating in Bulimia Nervosa and Binge Eating Disorder: A Three-Year Follow-Up Study. *Psychotherapy and Psychosomatics*, 81(1), 11-20.
- Claes, L., Nederkoorn, C., Vandereycken, W., Guerrieri, R., & Vertommen, H. (2006). Impulsiveness and lack of inhibitory control in eating disorders. *Eating Behaviors*, 7(3), 196-203.
- Crawford, J.R., Deary, I.J., Starr, J.M., & Whalley, L.J. (2001). The NART as an index of prior intellectual functioning: a retrospective validity study covering a 66-year interval. *Psychological Medicine*, 31, 451-458.
- Delis, D.C., Kaplan, E., & Kramer, J.H. (2001). *Delis-Kaplan Executive Function System (DKEFS): Technical Manual*. San Antonio, Texas: The Psychological Corporation.
- Derogatis, L.R. (1994). *SCL-90 R Administration, Scoring and Procedures Manual – Third Edition*. Minneapolis: National Computer Systems Inc.
- Derogatis, L.R. (2000). SCL-90-R. In A.E. Kazdin (Ed.), *Encyclopedia of psychology*, Vol. 7, (pp. 192-193): American Psychological Association, Oxford University Press.
- Derogatis, L.R., Lipman, R.S., & Covi, L. (1973). SCL-90, an outpatient psychiatric rating scale-preliminary report. *Psychopharmacology Bulletin*, 9, 13-28.
- Dudley, R., Kuyken, W., & Padesky, C.A. (2011). Disorder specific and trans-diagnostic case conceptualisation. *Clinical Psychology Review*, 31(2), 213-224.
- Egan, S.J., Wade, T.D., & Shafran, R. (2011). Perfectionism as a transdiagnostic process: A clinical review. *Clinical Psychology Review*, 31(2), 203-212.
- Engel, S.G., Corneliussen, S.J., Wonderlich, S.A., Crosby, R.D., le Grange, D., Crow, S., Klein, M., Bardone-Cone, A., Peterson, C., Joiner, T., Mitchell, J.E., & Steiger, H. (2005). Impulsivity and compulsivity in bulimia nervosa. *The International Journal Of Eating Disorders*, 38(3), 244-251.
- Fairburn, C.G., & Cooper, Z. (1993). The Eating Disorder Examination (twelfth edition). In C.G. Fairburn & G.T. Wilson (Eds.), *Binge Eating: Nature, Assessment and Treatment*, (pp. 317-360). New York: Guilford Press.
- Fairburn, C.G., Cooper, Z., & Shafran, R. (2003). Cognitive behaviour therapy for eating disorders: a "transdiagnostic" theory and treatment. *Behaviour Research and Therapy*, 41(5), 509-528.
- Ferreri, F., Lapp, L.K., & Peretti, C.S. (2011). Current research on cognitive aspects of anxiety disorders. *Current Opinion in Psychiatry*, 24(1), 49-54.
- Giel, K.E., Wittorf, A., Wolkenstein, L., Klingberg, S., Drimmer, E., Schönenberg, M., Rapp, A.M., Fallgatter, A.J., Hautzinger, M., & Zipfel, S. (In Press). Is impaired set-shifting a feature of "pure" anorexia nervosa? Investigating the role of depression in set-shifting ability in anorexia nervosa and unipolar depression. *Psychiatry Research*, <http://dx.doi.org.ezproxy.webfeat.lib.ed.ac.uk/10.1016/j.bbr.2011.03.031>.
- Gohier, B., Ferracci, L., Surguladze, S.A., Lawrence, E., El Hage, W., Kefi, M.Z., Allain, P., Garre, J.-B., & Le Gall, D. (2009). Cognitive inhibition and working memory in unipolar depression. *Journal of Affective Disorders*, 116(1-2), 100-105.
- Goldner, E.M., Geller, J., Birmingham, C.L., & Remick, R.A. (2000). Comparison of shoplifting behaviours in patients with eating disorders, psychiatric control

- subjects, and undergraduate control subjects. *Canadian Journal of Psychiatry. Revue Canadienne de Psychiatrie*, 45(5), 471-475.
- Goodman, W.K., Price, L.H., Rasmussen, S.A., & Mazure, C. (1989). The Yale-Brown Obsessive Compulsive Scale: II. Validity. *Archives of General Psychiatry*, 46(11), 1012-1016.
- Graver, C.J., & White, P.M. (2007). Neuropsychological effects of stress on social phobia with and without comorbid depression. *Behaviour Research and Therapy*, 45(6), 1193-1206.
- Guillaume, S., Sang, C.N.T., Jaussent, I., Raingeard, I., Bringer, J., Jollant, F., & Courtet, P. (2010). Is decision making really impaired in eating disorders? *Neuropsychology*, 24(6), 808-812.
- Heaton, R.K., Chelune, G.J., Talley, J.L., Kay, G.G., & Curtiss, G. (1993). *Wisconsin Card Sorting Test Manual: Revised and Expanded*. Florida: Psychological Assessment Resources Inc.
- Herrera-Guzman, I., Gudayol-Ferre, E., Jarne-Esparcia, A., Herrera-Abarca, J.E., Herrera-Guzman, D., Pero-Cebollero, M., & Guardia-Olmos, J. (2009). Comorbidity of anxiety disorders in major depressive disorder. A clinical trial to evaluate neuropsychological deficit. *The European Journal of Psychiatry*, 23(1), 5-18.
- Hudson, J.I., Hiripi, E., Pope, H.G., & Kessler, R.C. (2007). The Prevalence and Correlates of Eating Disorders in the National Comorbidity Survey Replication. *Biological Psychiatry*, 61(3), 348-358.
- Kemps, E., & Wilsdon, A. (2010). Preliminary evidence for a role for impulsivity in cognitive disinhibition in bulimia nervosa. *Journal of Clinical and Experimental Neuropsychology*, 32(5), 515-521.
- Kim, S.W., Dysken, M.W., & Kuskowski, M. (1992). The Symptom Check List 90: a reliability and validity study. *Psychiatry Research*, 41, 37-44.
- Kirisci, L., Tarter, R.E., Vanyukov, M., Reynolds, M., & Habeych, M. (2004). Relation between cognitive distortions and neurobehavior disinhibition on the development of substance use during adolescence and substance use disorder by young adulthood: a prospective study. *Drug and Alcohol Dependence*, 76(2), 125-133.
- Koeter, M.W.J. (1992). Validity of the GHQ and SCL anxiety and depression scales: A comparative study. *Journal of Affective Disorders*, 24(4), 271-279.
- Konstantakopoulos, G., Tchanturia, K., Surguladze, S.A., & David, A.S. (2011). Insight in eating disorders: clinical and cognitive correlates. *Psychological Medicine*, 41(09), 1951-1961.
- Kuelz, A.K., Hohagen, F., & Voderholzer, U. (2004). Neuropsychological performance in obsessive-compulsive disorder: a critical review. *Biological Psychology*, 65(3), 185-236.
- Langenecker, S.A., Zubieta, J.K., Young, E.A., Akil, H., & Nielson, K.A. (2007). A task to manipulate attentional load, set-shifting, and inhibitory control: Convergent validity and test-retest reliability of the Parametric Go/No-Go Test. *Journal of Clinical and Experimental Neuropsychology*, 29(8), 842-853.
- Lauer, C.J., Gorzewski, B., Gerlinghoff, M., Backmund, H., & Zihl, J. (1999). Neuropsychological assessments before and after treatment in patients with anorexia nervosa and bulimia nervosa. *Journal of Psychiatric Research*, 33(2), 129-138.

- Lyche, P., Jonassen, R., Stiles, T.C., Ulleberg, P., & Landro, N.I. (2011). Verbal memory functions in unipolar major depression with and without co-morbid anxiety. *The Clinical Neuropsychologist*, 25(3), 359-375.
- Martinez-Gonzalez, A.E., & Piqueras-Rodriguez, J.A. (2008). Neuropsychological update on obsessive-compulsive disorder. *Revista de Neurologia*, 46(10), 618-625.
- McClintock, S.M., Husain, M.M., Greer, T.L., & Cullum, C.M. (2010). Association between depression severity and neurocognitive function in major depressive disorder: a review and synthesis. *Neuropsychology*, 24(1), 9-34.
- Miles, J., & Shevlin, M. (2001). *Applying Regression and Correlation: a guide for students and researchers*. London: Sage Publications.
- Murphy, R., Nutzinger, D.O., Paul, T., & Leplow, B. (2004). Conditional-associative learning in eating disorders: a comparison with OCD. *Journal of Clinical and Experimental Neuropsychology*, 26(2), 190-199.
- Naylor, H., Mountford, V., & Brown, G. (2011). Beliefs about Excessive Exercise in Eating Disorders: The Role of Obsessions and Compulsions. *European Eating Disorders Review*, 19(3), 226-236.
- Nelson, H.E. (1982). *National Adult Reading Test (NART): Test Manual*. London: NFER Nelson Publishing Co Ltd.
- Nelson, H.E., & Willison, J. (1991). *National Adult Reading Test (NART). Test manual, 2nd*. London, UK: NFER-Nelson.
- NICE. (2004). Eating Disorders: Core interventions in the treatment and management of anorexia nervosa, bulimia nervosa and related eating disorders. *Clinical Guideline 9*. Available from www.nice.org.uk.
- O'Toole, M.S., & Pedersen, A.D. (2011). A systematic review of neuropsychological performance in social anxiety disorder. *Nordic Journal of Psychiatry*, 65(3), 147-161.
- Polak, A.R., Witteveen, A.B., Reitsma, J.B., & Olff, M. (2012). The role of executive function in posttraumatic stress disorder: A systematic review. *Journal of Affective Disorders*, in press/available online February 2012(0).
- Porter, R.J., Bourke, C., & Gallagher, P. (2007). Neuropsychological impairment in major depression: its nature, origin and clinical significance. *The Australian And New Zealand Journal Of Psychiatry*, 41(2), 115-128.
- Robbins, T.W., Gillan, C.M., Smith, D.G., de Wit, S., & Ersche, K.D. (2012). Neurocognitive endophenotypes of impulsivity and compulsivity: towards dimensional psychiatry. *Trends in Cognitive Sciences*, 16(1), 81-91.
- Roberts, M.E., Tchanturia, K., Stahl, D., Southgate, L., & Treasure, J. (2007). A systematic review and meta-analysis of set-shifting ability in eating disorders. *Psychological Medicine*, 37(8), 1075-1084.
- Roberts, M.E., Tchanturia, K., & Treasure, J.L. (2010). Exploring the neurocognitive signature of poor set-shifting in anorexia and bulimia nervosa. *Journal of Psychiatric Research*, 44(14), 964-970.
- Robinson, M.D., Pearce, E.A., Engel, S.G., & Wonderlich, S.A. (2009). Cognitive Control Moderates Relations Between Impulsivity and Bulimic Symptoms. *Cognitive Therapy and Research*, 33(4), 356-367.
- Rosval, L., Steiger, H., Bruce, K., Israël, M., Richardson, J., & Aubut, M. (2006). Impulsivity in women with eating disorders: problem of response inhibition,

- planning, or attention? *The International Journal Of Eating Disorders*, 39(7), 590-593.
- Ruuska, J., Kaltiala-Heino, R., Rantanen, P., & Koivisto, A.-M. (2005). Psychopathological distress predicts suicidal ideation and self-harm in adolescent eating disorder outpatients. *European Child and Adolescent Psychiatry*, 14(5), 276-281.
- Southgate, L., Tchanturia, K., & Treasure, J. (2008). Information processing bias in anorexia nervosa. *Psychiatry Research*, 160(2), 221-227.
- Steketee, G., Frost, R., & Bogart, K. (1995). The Yale-Brown obsessive compulsive scale: interview versus self report. *Behaviour Research and Therapy*, 34(8), 675-684.
- Tabachnick, B.G., & Fidell, L.S. (2001). *Using Multivariate Analysis* (Vol. 4th edition). Boston: Allyn and Bacon.
- Tchanturia, K., Davies, H., & Campbell, I.C. (2007). Cognitive remediation therapy for patients with anorexia nervosa: preliminary findings. *Annals of General Psychiatry*, 6(14).
- Tchanturia, K., Anderluh, M.B., Morris, R.G., Rabe-Hesketh, S., Collier, D.A., Sanchez, P., & Treasure, J.L. (2004). Cognitive flexibility in anorexia nervosa and bulimia nervosa. *Journal of the International Neuropsychological Society*, 10(4), 513-520.
- Tchanturia, K., Morris, R.G., Anderluh, M.B., Collier, D.A., Nikolaou, V., & Treasure, J. (2004). Set shifting in anorexia nervosa: an examination before and after weight gain, in full recovery and relationship to childhood and adult OCPD traits. *Journal of Psychiatric Research*, 38(5), 545-552.
- Van den Eynde, F., Guillaume, S., Broadbent, H., Stahl, D., Campbell, I.C., Schmidt, U., & Tchanturia, K. (2011). Neurocognition in bulimic eating disorders: a systematic review. *Acta Psychiatrica Scandinavica*, 124(2), 120-140.
- Verdejo-García, A., Bechara, A., Recknor, E.C., & Pérez-García, M. (2006). Executive dysfunction in substance dependent individuals during drug use and abstinence: An examination of the behavioral, cognitive and emotional correlates of addiction. *Journal of the International Neuropsychological Society*, 12(03), 405-415.
- Wechsler, D. (1981). *Wechsler Adult Intelligence Scale-Revised (WAIS-R)*: The Psychological Corporation.
- Woody, S.R., Steketee, G., & Chambless, D.L. (1995). Reliability and validity of the Yale-Brown Obsessive Compulsive Scale. *Behaviour Research and Therapy*, 33, 597-605.
- Xu, G., Lin, K., Rao, D., Dang, Y., Ouyang, H., Guo, Y., Ma, J., & Chen, J. (2012). Neuropsychological performance in bipolar I, bipolar II and unipolar depression patients: A longitudinal, naturalistic study. *Journal of Affective Disorders*, 136(3), 328-339.
- Zakzanis, K.K., Campbell, Z., & Polsinelli, A. (2010). Quantitative evidence for distinct cognitive impairment in anorexia nervosa and bulimia nervosa. *Journal Of Neuropsychology*, 4(Pt 1), 89-106.
- Zigmond, A., & Snaith, R. (1983). The Hospital Anxiety and Depression Scale. *Acta Psychiatrica Scandinavica*, 67, 361-370.

Chapter 5: Methodology

The methodology outlined in this chapter is based on clinical guidelines and best research practice for eating disorder populations, self harm and those with diagnoses of anxiety or depression (NHS QIS, 2006; NICE, 2004a, 2004b, 2010, 2011).

5.1 Design

The current study incorporated a quantitative framework with a between groups cross sectional design. Data were collected using formal neuropsychological testing, questionnaires and interview. The study was designed to address methodological limitations recently highlighted by a systematic review of the current literature relating to neuropsychological correlates of bulimia nervosa (Van den Eynde *et al.*, 2011). Design features addressing these limitations include use of a comparison group to address the issue of specificity and potentially confounding comorbidities, reporting of effect sizes within results and using measures already reported on within the literature in order to facilitate comparisons between studies.

In addition, this project was designed within the context of the Tayside Eating Disorder Research Group to complement recent research relating to neuropsychological correlates of inpatients and outpatients with anorexia.

5.2 Participants

5.2.1 Inclusion/exclusion criteria

The inclusion/exclusion criteria for each group; outpatients with Bulimia Nervosa or Eating Disorder Not Otherwise Specified with bulimic features (EDNOS-BN), and outpatients with anxiety and/or depression, are listed below.

Group 1: Outpatients with Bulimia Nervosa or EDNOS-BN

Inclusion Criteria:

- Female
- English speaking
- Age 18-65

- Meet DSM-IV criteria for a diagnosis of Bulimia Nervosa or EDNOS-BN (or ICD 10 criteria for Bulimia Nervosa or Atypical Bulimia, excluding Binge Eating Disorder¹)
- Receiving treatment for Bulimia Nervosa or EDNOS-BN on an outpatient basis as part of NHS Tayside or NHS Grampian Eating Disorder Services

Exclusion Criteria:

- Medically unstable
- Current diagnosis of Anorexia Nervosa
- Psychosis
- Previous inpatient treatment for their eating disorder
- History of Learning Disability/Developmental Disorder
- History of head injury involving loss of consciousness
- History/current Neurological Disorder
- Uncorrected significant visual or motor impairment
- Past substance abuse/related disorder
- Knowledge of Neuropsychological tests

Group 2: Outpatients with Anxiety and/or Depression

Inclusion Criteria:

- Female
- English speaking
- Age 18-65
- Meet DSM-IV criteria for Anxiety or Major Depression (any Anxiety disorder was acceptable as long as HADS scores were in the clinical range)
- Score 11 or above on either the anxiety or depression scale of the HADS
- Receiving treatment for anxiety and/or depression at primary care in Tayside

¹ ICD 10 criteria were used by recruiting clinicians in Grampian, further explained in Chapter 3

Exclusion Criteria:

- History of Learning Disability/Developmental Disorder
- Significant current Medical/Psychiatric Disorder. Significant psychiatric disorder is identified if the individual is receiving treatment from specialist mental health services for a disorder.
- Any significant suicidal ideation or intent
- History of head injury involving loss of consciousness
- History/current Neurological Disorder
- Uncorrected significant visual or motor impairment
- Past substance abuse/related disorder
- EDE score above 4
- Knowledge of Neuropsychological tests

5.2.2 The BN Group: Outpatients with Bulimia Nervosa or EDNOS-BN

The BN group consisted of 21 female outpatients meeting the inclusion and exclusion criteria, as defined in Section 5.2.1, who were recruited from NHS Tayside and NHS Grampian Eating Disorder Services. Demographic characteristics of the sample are primarily described in the journal article in Chapter 4 (Table 4.2). Additional information on descriptive categorical variables is provided in Table 5.1.

5.2.2.1 Identification of Participants

Potential participants were identified by their treating clinicians within the Eating Disorders Services, as those they felt were medically and psychiatrically fit to participate in the study. Treating clinicians were Clinical Psychologists, Clinical Associates in Applied Psychology or Senior Nurse Specialists. Clinicians offered these patients the Participant Information Sheet and briefly discussed the study with them. For most participants, this information was provided during a therapy appointment. A number of potentially suitable participants in Grampian were informed of the study by letter by their clinician, as there was a long time lapse between appointments within the service. The letter text is reproduced in Appendix 7. The Participant Information Sheet was enclosed (Appendix 8), along with a short description of the procedure. Contact information was provided in the event that the patient wished to participate or to seek further information.

Participation was voluntary and patients were informed that their choice to participate or not would have no affect on their treatment. 29 patients were offered study information by clinicians in Dundee and approximately the same number in Grampian, although exact numbers could not be obtained at the time of writing. Twenty nine patients agreed to be contacted by the researcher. Of these, 2 dropped out before testing, 4 were unavailable, 1 was excluded for dyslexia and 1 for previous electroconvulsive therapy

As described in the Introduction Chapter (Chapter 1), male patients were not included in this study, which allows the sample to be directly comparable to existing key papers that have used only female participants.

5.2.3 The AD Group: Outpatients with Anxiety and/or Depression

The AD group consisted of 23 female outpatients being treated for anxiety disorders and/or Major Depressive Disorder (MDD) within NHS Tayside Adult Psychological Therapies Services. All participants met inclusion and exclusion criteria as set out in Section 5.2.1. Demographic characteristics of the sample are primarily described in the journal article in Chapter 4 (Table 4.2). Additional information on descriptive categorical variables is provided in Table 5.1.

Although difficulties with set shifting and cognitive inhibition ability have been found in patient groups with symptoms of anxiety and depression, results have been mixed, as described in Chapter 4. This group was included as a clinical comparison group to investigate if deficits which have been reported in BN are shared with other common psychological disorders.

5.2.3.1 Identification of Participants

Potential participants were identified by clinicians in the same way as patients with BN. All Clinical Psychologists, Counselling Psychologists, CBT therapists and Clinical Associates in Applied Psychology working with the Angus, Dundee and Perth Adult psychological therapies services were informed of the study and asked to consider if patients on their caseload may be suitable. As a large number of participants were sought and the time commitment was expected to discourage some potential participants, a large number of patients were invited to participate.

Approximately 100 patients were offered study information by clinicians. The Dundee Adult Psychological Therapies team reported 50 patients invited to participate, the Angus Adult Psychological Therapies team reported 29 patients invited to participate and the Perth Adult Psychological Therapies team were unable

to report an accurate number. If an approximate number of 30 patients invited to participate is estimated for the Perth team, the total number of patients invited to participate in the AD group was approximately 109. In total, 37 patients agreed to be contacted by the researcher. Of these, 9 were ultimately unavailable to participate, 2 were excluded for dyslexia, 1 for having poor quality spoken English, 1 did not meet inclusion criteria related to the HADS and 1 was unavailable for 2 consecutive hours.

5.3 Additional Descriptive data for BN and AD groups

The main participant characteristics are described in Chapter 4, Table 4.2. Table 5.1 below provides further information on descriptive data for both groups. No significant differences were found between the groups on handedness, the amount of time since they had last eaten or the report of any birth related complications. Similar proportions of each group were current alcohol and medication users. No one in either group was a current illegal drug user.

Table 5.1: Demographic information for categorical data in Bulimic and Anxious/Depressed group

	Bulimic Group n=21		Anxious/Depressed Group n=23		Fisher's exact test <i>p</i>
	<i>N</i>	%	<i>n</i>	%	
Handedness					
Right	19	90	17	74	.432
Left	1	5	4	17	
Ambidextrous	1	5	2	9	
Time Last Eaten					.369
Within 3 hours	13	62	16	70	
3-6 hours ago	1	5	3	13	
6-24 hours	7	33	4	17	
Current Alcohol User	18	86	17	74	.462
Current Drug User	0	0	0	0	.999
Currently Taking Medication	11	52	15	65	.541
Pre/Post Natal Complications	8	38	8	35	.999

5.4 Measures

5.4.1 Psychological Measures

Psychological Measures used are listed in Table 5.2.

Table 5.2 Psychological Measures

Psychological Measure	Areas Assessed
Hospital Anxiety and Depression Scale (HADS)	Current anxiety and depressive symptoms
Eating Disorders Examination (EDE)	Eating psychopathology
Symptom Check List–90 Revised (SCL–90R)	General psychopathology
Self Liking/Self Competence Scale	Self esteem
Yale–Brown Obsessive-compulsive Scale (Y–BOCS)	Obsessive and compulsive symptoms
Social Problem Solving Inventory Revised (SPSI–R)	Social problem solving ability

5.4.1.1 Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983)

The HADS is a self-report measure of experienced anxiety and depression, which has been used extensively in clinical studies (Bjelland *et al.*, 2002). It contains an anxiety and a depression scale, each consisting of 7 questions with 4 possible responses relating to the severity of the symptom in question. The response is translated into a score from 0 to 3 for each question. The anxiety and depression scores are categorised individually as normal (0-7), mild (8-10), moderate (11-14) and severe (15-21). The HADS was administered to adult outpatients as part of routine clinical practice and ongoing review.

The HADS depression subscale has 90% sensitivity and 86% specificity for depression compared to the gold standard of a structured diagnostic interview (Zigmond & Snaith, 1983). Crawford, Henry *et al.* (2001) reported the reliability of the HADS as acceptable and the subscales moderately correlated (0.53). A recent

review by Bjelland *et al.* (2002) reported the reliability of the Anxiety subscale to vary from 0.68 to 0.93 (mean 0.83) and for the Depression subscale from 0.67 to 0.90 (mean 0.82).

5.4.1.2 Eating Disorders Examination (EDE) Version 12 (Fairburn & Cooper, 1993)

The EDE is a semi-structured, investigator based clinical interview that is generally regarded as the ‘gold standard’ instrument for measuring eating disordered attitudes and behaviours. It contains 23 items rated in regards to the past 28 days on a 7-point Likert scale, ranging from ‘0’ (‘not at all’) to ‘6’ (‘markedly’ or ‘every day’), with higher scores indicating more severe eating pathology. Responses are used to calculate four subscales (Dietary Restraint, Eating Concern and Weight Concern, each ranging from 0-30, and Shape Concern, ranging from 0-48), and a global score (mean of the 4 subscales). All subscale mean scores and the global score range from 0-6. The EDE can also be used as a diagnostic tool for DSM-IV, containing frequency measures of binge eating and compensatory behaviours.

Good internal consistency, (Beumont *et al.*, 1993; Cooper *et al.*, 1989) concurrent (Rosen *et al.*, 1990) and discriminant (Cooper *et al.*, 1989; Rosen *et al.*, 1990; Wilson & Smith, 1989) validity, and inter-rater reliability (Black & Wilson, 1996; Cooper & Fairburn, 1987; Rosen *et al.*, 1990; Wilson & Smith, 1989) have been demonstrated for the EDE in adults. It also discriminates well between different types of eating disorder (Beumont *et al.*, 1995; Fairburn & Cooper, 1993) .

5.4.1.3 Symptom Check List-90 Revised (SCL-90R) (Derogatis, 1994; Derogatis *et al.*, 1973)

The SCL-90R is a 90-item self-report instrument for measuring general psychopathology for use with community, medical and psychiatric respondents. It contains 90 problem items rated in regards to the past 7 days on a 5-point Likert scale of distress from 0 ‘Not at All’ to 4 ‘Extremely’. It comprises nine primary symptom dimensions - Somatisation, Obsession-Compulsion, Interpersonal

Sensitivity, Depression, Anxiety, Hostility, Phobic Anxiety, Paranoid Ideation and Psychoticism – for which mean scores (range 0-4) are calculated. An ‘Additional’ scale is also included in the measure which contains a collection of symptom items relating to disturbed sleep, feelings of guilt, overeating, thoughts of death and poor appetite.

Responses to these subscales are used to calculate three global indices: the Global Severity Index (GSI), the Positive Syndrome Distress Index (PSDI) and the Positive Symptom Total (PST). The GSI is the mean value of all the items (total divided by 90). GSI thus ranges from 0-4. The PST is the number of items which have been scored higher than zero. PST thus ranges from 0-90. The PSDI is the total sum of all ratings divided by the PST, and ranges from 0-4.

Good internal consistency of the primary symptom dimensions and global indices has been demonstrated across a number of populations including control groups (Derogatis, 1983), psychiatric inpatients (Rauter *et al.*, 1996), and substance abuse inpatients (Zack *et al.*, 1998) as well as cancer patients (Fitch *et al.*, 1995). Alpha coefficients have ranged from 0.77 to 0.90 in one study of 209 symptomatic volunteers (Derogatis *et al.*, 1976) and from 0.79 to 0.90 with a sample of psychiatric outpatients (Horowitz *et al.*, 1988). More recently, similar results have been found with Cronbach’s alpha coefficient ranging from 0.77 for the Hostility subscale to 0.90 for the Somatisation and Depression subscales among psychiatric outpatients in Finland (Holi, 2003; Holi *et al.*, 2003). The SCL-90-R has been found to have good test-retest reliabilities across a range of patient groups and test-retest intervals (Derogatis, 2000). Therefore, previous completion of the SCL-90-R was acceptable among participants. Good convergent-discriminant validity for the SCL-90R has also been demonstrated in patients and healthy controls (Boleloucky & Horvath, 1974; Derogatis *et al.*, 1976; Peveler & Fairburn, 1990); however examination of the convergent and discriminant validity of the subscales has produced mixed results. The Depression and Anxiety subscales have the most evidence of convergent and discriminant validity (Bech *et al.*, 1992; Derogatis, 2000; Koeter, 1992). The Obsession-Compulsion subscale has been shown to be internally consistent (Woody *et al.*, 1995) but has also been found to have poor discriminant validity (Kim *et al.*,

1992; Woody *et al.*, 1995). The SCL-90 has been used in BN patient groups to assess general psychopathology (Brand *et al.*, 2007; Fairburn *et al.*, 2007; Krug *et al.*, 2008), and found to have good concurrent validity within a BN patient group using comparison with an investigator based interview, the Present State Examination (Peveler & Fairburn, 1990).

Scores for all scales were recorded for the purpose of comparison between the two groups on psychological distress. The symptoms dimensions of Depression, Obsession-Compulsion and Anxiety were used in the investigation of the relationship between psychopathology and performance on neuropsychological tasks of set shifting and inhibition.

5.4.1.4 Self-Liking/Competence Scale (Revised) (SLCS-R) (Tafarodi & Swann, 2001)

The SLSC-R is a 16 item measure of two-dimensional self-esteem composed of two interdependent subscales of self liking and self competence. It contains 8 items relating to self worth and self competence and 8 items relating to sense of self-efficacy. Participants rate the items on a 5-point Likert scale ranging from 1 (*strongly disagree*) to 5 (*strongly agree*). The item scores are then summed and combined into an overall subscale score. These can range from 8 to 40, with higher scores indicating higher self-competence or higher self-liking. It has been tested for discriminant and convergent validity and found to constitute best fit on all indices, when compared to other self esteem measures. Reliability and validity of a translated version of the questionnaire were found to be appropriate in a Dutch sample (Vandromme *et al.*, 2007). Internal consistency was found to be good in an American sample, with alpha coefficients of 0.90 for Self-Liking and 0.82 for Self-Competence (Mar *et al.*, 2006). Self competence has also been found to correlate with eating pathology in a recent study (Paterson *et al.*, 2007).

5.4.1.5 Yale-Brown Obsessive Compulsive Scale-Symptom Check List (Y-BOCS-SC) (Goodman, Price, Rasmussen, & Mazure, 1989).

Regarded as the 'gold standard' for the assessment of obsessive compulsive symptoms, (Deacon & Abramowitz, 2005; Frost *et al.*, 1995; Moritz *et al.*, 2002), the YBOCS consists of a 58 item symptom checklist and a 10 item severity scale. The symptom checklist covers a range of obsessions and compulsions, clustered by behavioural expression (e.g. checking compulsions) and thematic content (e.g. contamination obsessions). Obsessions and compulsions are assessed over the 5 dimensions of time spent, interference in functioning, distress, efforts to resist and perceived control, creating a 10-item severity measure.

Respondents used the symptom checklist to identify their main symptoms and then completed the YBOCS severity scale with these in mind, in relation to the past 7 days. Items are rated on a 5-point scale from 0 (no symptoms) to 4 (extreme symptoms.) The symptom checklist is not scored. Scores on the YBOCS thus range from 0-40 with higher scores indicating more severe OCD symptoms.

The YBOCS can be administered in the form of interview or self-report. There are small differences between the two versions, such as the inclusion of plain-language explanations of the concepts and the removal of an 'other' option in the symptom checklist. A number of studies have demonstrated the validity and reliability of the interview version (Goodman, Price, Rasmussen, & Mazure, 1989; Goodman, Price, Rasmussen, Mazure, *et al.*, 1989; Kim *et al.*, 1990; Woody *et al.*, 1995). Comparison of interview and self-report administration showed moderate to good agreement between both the symptom checklist and severity ratings, with Federici *et al.* (2010) noting that the compulsions scales were more highly correlated between versions than were the obsessions scales (Steketee *et al.*, 1995). The current study uses a self-report version of the YBOCS (Baer, 1991) which was also used by Federici *et al.* (2010). The YBOCS has been used to measure obsessive and compulsive symptoms in bulimic patients in a number of studies (Kaye, 2005; Matsunaga *et al.*, 1999; Murphy *et al.*, 2004; Roberts *et al.*, 2010).

5.4.1.6 Social Problem Solving Inventory Revised (SPSI-R) (D'Zurilla *et al.*, 1998)
(D'Zurilla & Maydeu-Oliveres, 1995)

The SPSI-R is a 52-item, multidimensional, self-report measure of social problem solving ability. Each item is rated on a five-point scale from 0 'not at all true of me' to 4 'extremely true of me'. The SPSI-R comprises two problem orientation measures (positive problem orientation, negative problem orientation) and three actual problem-solving measures (rational problem-solving, impulsivity/carelessness style, avoidance style), as described in Table 5.3.

Table 5.3 Subscales of the SPSI-R

Subscale	Attitudes and Behaviours Measured
Problem Orientation	
Positive Problem Orientation (PPO)	Positive appraisal, self-efficacy and outcome expectancies.
Negative Problem Orientation (NPO)	Dysfunctional cognitive processes, threat perception and frustration tolerance.
Problem Solving	
Rational Problem Solving (RPS)	Systematic problem solving, realistic goal setting and evaluating outcomes
Impulsivity/Carelessness Style (ICS)	Impulsive, incomplete or careless problem solving strategies
Avoidance Style (AS)	Procrastination, passivity and inaction

The problem solving subscales of the SPSI-R have been shown to accurately predict academic success after controlling for aptitude, indicating ecological validity of the subscales (D'Zurilla & Sheedy, 1992). Acceptable convergent, construct and discriminant validity have been reported among psychiatric inpatients and healthy adults (Chang & D'Zurilla, 1996; D'Zurilla *et al.*, 1998; D'Zurilla & Maydeu-Oliveres, 1995). Test-retest reliabilities range from 0.72 for positive problem orientation to 0.88 for negative problem orientation (D'Zurilla *et al.*, 1998).

The negative problem orientation and avoidance subscales have been linked to eating pathology in anorexia (Paterson *et al.*, 2007). These scales have also been linked to depressive symptoms (Klein *et al.*, 2011; Londahl *et al.*, 2005). Negative problem orientation has also been found to be a significant predictor of worry after controlling for trait anxiety (Belzer *et al.*, 2002).

5.4.2 Neuropsychological Measures

As executive function describes a broad spectrum of cognitive abilities, and tests of executive function have been shown to require the use of a number of cognitive functions simultaneously, it is difficult to isolate an ability such as set shifting or inhibition in any one task (Burgess, 2003). Many studies have consistently reported varying performance among their subjects on neuropsychological tests which measure similar constructs (for example in BN samples; Alvarez-Moya *et al.*, 2009; Brand *et al.*, 2007; Tchanturia, Morris, *et al.*, 2004). For these reasons the test battery contained a number of measures designed to access set shifting and cognitive inhibition ability but which necessarily also overlap with other executive functions.

Table 5.4 Neuropsychological Measures and Primary Areas Assessed

Neuropsychological Measures	Primary Areas Assessed
National Adult Reading Test (NART)	Pre-morbid intellectual ability
Delis–Kaplan Executive Function System (DKEFS) Trail Making Task	Attention, Set shifting, cognitive flexibility
Delis–Kaplan Executive Function System (DKEFS) Verbal Fluency	verbal fluency Cognitive flexibility, set shifting (condition 3),
Delis–Kaplan Executive Function System (DKEFS) Colour-Word Interference	Response inhibition, (also set shifting in condition 4)
Hayling Test	Response inhibition
Brixton Test	Set shifting
Wisconsin Card Sort Test (WCST)	Set shifting, category formation and set maintenance

5.4.2.1 National Adult Reading Test (NART) (Nelson, 1982; Nelson & Willison, 1991)

The NART is a measure of premorbid intellectual ability. The participant is asked to read aloud 50 irregularly spelt words (e.g. cough). The number of pronunciation errors is recorded and used to estimate the Wechsler Adult Intelligence Scale (WAIS-R; Wechsler, 1981) score from standardised norms. The NART's validity as a measure of premorbid intelligence has been well documented (e.g. Crawford, Deary, *et al.*, 2001). Recently Bright *et al.* (2002) demonstrated that neither the use of demographic variables or a combination of NART score and demographic variables was significantly better than NART scores at estimating premorbid IQ. NART performance remains preserved despite a number of cognitive impairments, however its preservation in some disorders, such as Alzheimer's and Huntington's disease has been questioned. The NART has demonstrated good internal consistency (Crawford *et al.*, 1988; Nelson & Willison, 1991), test-retest reliability, and inter-rater reliability (Crawford *et al.*, 1989). The NART has been used as a measure of premorbid IQ in eating disordered patients in a number of neuropsychological studies (Guillaume *et al.*, 2010; Lopez *et al.*, 2008; Tchanturia, Morris, *et al.*, 2004; Van den Eynde *et al.*, 2012).

5.4.2.2 Delis-Kaplan Executive Function System (D-KEFS) (Delis *et al.*, 2001)

Three tests from the D-KEFS were used:

Verbal Fluency Test – This is a measure of spontaneous production of words in conditions of letter fluency (FAS, condition 1), category fluency (Animals and Boys names, condition 2) and a category switching condition where a participant must switch between naming items from each of 2 categories (Fruits and Furniture, condition 3). In each condition, the score is the total number of correct responses generated in 60 seconds.

FAS test-retest reliability and inter-rater reliability were found to be good by Vlaar and Wade (2003). Test-retest reliability for D-KEFS category fluency is 0.79 (Delis

et al., 2001). The inter-rater reliability for general category fluency tasks is very good (Spreen & Strauss, 1998). Good internal consistency has been reported for the verbal fluency component and category switching component in the D-KEFS manual (Delis *et al.*, 2001). Performance of BN patients on the FAS task is not different to controls according to the current literature (Brand *et al.*, 2007; Tchanturia, Anderluh, *et al.*, 2004). However, the switching element of condition 3 in the D-KEFS is not a component of the standard verbal fluency task, which usually only includes a letter and category fluency task (Lezak *et al.*, 2004). This switching task may highlight difficulties in set shifting in individuals with BN.

Colour Word Inference Test – This is a measure of selective attention and response inhibition. The Stroop test, which is a longstanding test of cognitive flexibility and inhibition, has been modified in the D-KEFS battery to include a baseline colour naming condition (condition 1) and a set shifting condition (Colour Word Inhibition Switch, condition 4) in addition to the traditional colour word reading (condition 2) and colour word interference tasks (condition 3). In each condition, the outcome measures are the time taken to read 50 items and the number of errors made. Good internal consistency and test-retest reliability has been reported (Delis *et al.*, 2001). Colour word interference 3 has been identified as an a priori key variable as significant differences have been found on this measure between samples of people with BN and healthy controls (Kemps & Wilsdon, 2010).

Trail Making Test (TMT) – This test assesses planning and cognitive flexibility. There are 5 conditions in the D-KEFS TMT in contrast to the 2 conditions in the traditional TMT. The five conditions are visual scanning (condition 1), number sequencing (condition 2), letter sequencing (condition 3), number-letter switching (condition 4), and motor speed (condition 5). The procedure for the first condition involves a timed visual search. The remaining conditions involve drawing a line connecting the target items (numbers, letters or empty circles) as quickly as possible while ignoring distracter items. The switching task involves switching back and forth between connecting numbers and letters, completing the task as quickly as possible. In each condition, the outcome measures are time to complete task and

number of errors. Good internal consistency and moderate test-retest reliability are described in the technical manual (Delis *et al.*, 2001). TMT4 completion time and TMT4 number of errors were identified as key variables, due to significant differences between BN patients and healthy controls found on these subscales in recent studies (Brand *et al.*, 2007; Konstantakopoulos *et al.*, 2011; Roberts *et al.*, 2010; Tchanturia, Morris, *et al.*, 2004).

5.4.2.3 Hayling & Brixton (Burgess & Shallice, 1997)

The Hayling and Brixton tests measure behavioural regulation, including response inhibition and set shifting.

The Hayling test evaluates initiation speed, by first requiring participants to logically complete 15 sentences as quickly as possible. The second part of the task requires them to complete 15 sentences with unrelated words as quickly as possible, which is a measure of response suppression. The sum of time to respond and total number of errors are the outcome measures. The number of errors in the Hayling test part 2 was chosen as an a priori key measure as a composite value using this measure described significant differences between people with BN and healthy controls (Kemps & Wilsdon, 2010).

The Brixton test is a concept formation and set shifting task. The test consists of 56 pages, each consisting of the same array of ten circles numbered 1–10 (one circle coloured blue). Participants are asked to predict the movement of the blue circle from page to page by detecting a logical pattern from previous pages. The pattern changes 8 times during the task and the participant has to determine the new pattern. The outcome measure is the total number of incorrect predictions made. No differences have been found to date between patients with BN and healthy controls on this task (Roberts *et al.*, 2010; Tchanturia, Anderluh, *et al.*, 2004; Van den Eynde *et al.*, 2011).

The technical manual reports the test-retest reliabilities for both tasks as adequate (Burgess & Shallice, 1997). Adequate inter-rater reliability was reported for the Hayling test by Andres and Van der Linden (2000) .

5.4.2.4 Wisconsin Card Sort Test (WCST) (Heaton *et al.*, 1993)

The WCST is one of the most widely used tasks in the assessment of cognitive function. It measures the aspects of executive function thought to be related to the frontal lobes, such as concept formation, set-shifting, and set maintenance. The WCST was administered in the standardized format (Heaton *et al.*, 1993). Four stimulus ‘key cards’ with symbols differing in colour, shape and number are placed in front of the participant, who is given a pack of 128 response cards and instructed to match each response card to one of the key cards by placing it on the table under that key card. The researcher informs the participant whether each pairing is correct or incorrect. The participant’s aim is to match cards according to the current criterion. After coupling 10 cards with the first criterion (colour), the subject is required to shift to the second one (shape) and then to the third one (number). The procedure is repeated twice or until all 128 cards have been used. The official computerised scoring package was used to compute scores.

Test-retest reliabilities for the WCST have been examined by Heaton *et al.* (1993) and reported as ranging from 0.39 to 0.72. Bowden *et al.* (1998) reviewed these data and investigated reliability in an alcoholic and student population leading them to report a lower test-retest reliability of 0.22 to 0.55. Although previous literature had expected large practice effects to be seen in the WCST, these were not present in Bowden *et al.*’s (1998) data (Franzen, 1989). Ingram *et al.* (1999) also reported similar test-retest reliability 0.34 to 0.83 (mean=0.64) among sleep apnoea patients. Participants in the current study are unlikely to have encountered the WCST before and re-testing is not part of the procedure. Variable values for inter-rater reliability have been reported, ranging from excellent (Axelrod *et al.*, 1992) to quite low correlations (Flashman *et al.*, 1991).

Number of Perseverative errors, categories completed and non-perseverative errors were identified as a priori key measures based on significant findings related to these variables found in BN patient groups in studies by Roberts *et al.* (2010) and Alvarez-Moya *et al.* (2009). A perseverative error is one where the participant continues to sort the cards in the same way, after the examiner says the card is wrong or changes criteria. Number of categories completed is the number of runs of 10 correct responses in a row (max. 6). A non-perseverative error is any error not categorised as a Perseverative error. Non-perseverative errors have been hypothesised to contain both efficient errors, which are used to test out and establish the new criterion, and inefficient errors, which have been linked to disinhibition and distraction in responding (Alvarez-Moya *et al.*, 2009; Barceló & Knight, 2002).

5.5 Procedure

A diagram representing the participant journey from being approached by clinical staff to completion of participation is shown in Figure 5.1.

Group 1: Bulimia/Atypical Bulimia

Group 2: Anxious/Depressed

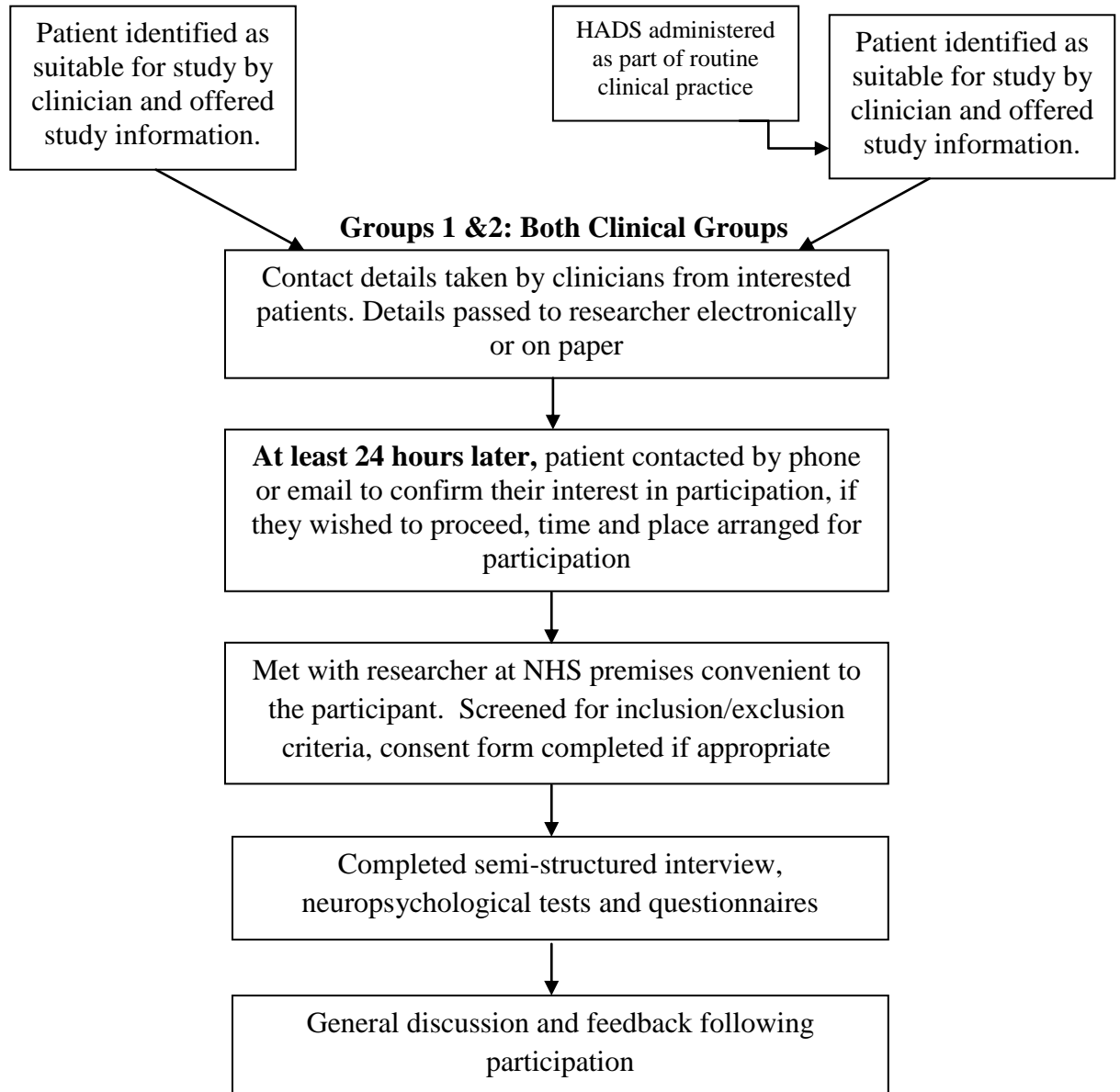


Figure 5.1 Participant Journey

5.5.1 The BN Group: Patients with Bulimia/EDNOS-BN

Study Sites: NHS Tayside Eating Disorder Service and Grampian Eating Disorder Service

Any outpatients attending NHS Tayside Eating Disorders Service, NHS Grampian Eating Disorders Service or NHS Tayside Adult Psychological Therapies Services

for treatment of an Eating Disorder and meeting inclusion criteria for the BN group were considered for participation in the study. The Adult Psychological Therapies pathway was ultimately not used for the BN group as the department was transitioning to a model where all eating disordered patients were transferred to the Eating Disorder Service.

Participants were recruited to the study through their treating clinician, as described in section 5.2.2.1. Patients with a possible interest in participation were given verbal and written information about the study by their clinician (Appendix 8). This information included details of the researcher's clinical supervisor within NHS Tayside Department of Clinical Neuropsychology, who could be contacted for further information. Patients who expressed a wish to participate and gave consent for their contact details to be passed on to the researcher, were given 24 hours to consider the information provided. When contacted by the researcher, participants were asked if they still had an interest in taking part. Most participants chose to give telephone contact details but email contact details were also used. Previous research has used similar methodology to contact potential participants and has demonstrated a high response rate (Crombie *et al.*, 2008; Kiezebrink *et al.*, 2009).

Patients wishing to participate met with the researcher in a clinic room at NHS premises convenient to their location within Tayside or Grampian. At the meeting, patients were given the opportunity to ask any further questions, screened for inclusion/exclusion criteria and if these were met, completed consent forms. They were informed that their participation was confidential and that they could withdraw from the study at any time without giving a reason.

The research procedure consisted of a semi-structured interview, to collect demographic information, and administration of the Eating Disorder Examination (EDE), which took 20 to 30 minutes. This was followed by formal neuropsychological testing in the order indicated in Table 5.2. Following this, a break was offered and then the remaining questionnaires were completed.

Neuropsychological tests lasted on average 45 to 60 minutes and the 4 questionnaires took approximately 20-30 minutes to complete.

Following completion of the measures, the researcher discussed with the participant her feelings about the experience of participation and any concerns or questions she had. In addition, items of the YBOCS and SCL-90-R relating to thoughts of death and self harm were checked by the researcher. If such items were endorsed, the researcher discussed with the participant their current levels of risk and support. If the researcher identified an unmet need for support, a protocol was in place to contact a clinical supervisor for further advice (see section 5.6.4).

5.5.2 The AD Group: Patients being treated for anxiety or depressive disorders in the Adult Psychological Therapies Service

Any outpatients attending NHS Tayside Adult Psychological Therapies Services for treatment of anxiety or depressive symptoms and meeting inclusion criteria for the comparison group were considered for participation in the study. Participants were recruited and testing administered as described in section 5.5.1.

5.5.3 Recruitment activity at the level of clinicians

Recruitment procedure was designed using recommendations from current literature, involving close collaboration with recruiting colleagues, regular feedback to them and using these discussions to consider the impact of study design on recruitment (Patel *et al.*, 2003). The researcher met with clinical teams before recruitment began, presenting information about the background, rationale and procedure for the study at team meetings. Meetings were attended periodically during the study and the researcher was in regular contact with the teams by email, including through reminder emails and recruitment updates to clinical leads. Clinical teams were also provided with updated feedback at intervals on the numbers of participants recruited. In addition, various methods were used to encourage recruitment within the teams, such as placement of reminder posters in team areas, placing study information in

clinic rooms or placing study information in patient files with coloured reminders pinned to the exterior of files.

Clinician workload in recruiting was minimised to identification of suitable participants and provision of study information for the BN group and additionally, the use of the HADS questionnaire to establish inclusion criteria for the AD group. Low clinician workload related to a study has been found to be associated with increased referral to Randomised Controlled Trials (B. Fletcher *et al.*, 2012). Clinicians were told that telephone numbers were the preferred method of contact, as previous experience and Cochrane reviews of literature on recruitment have indicated that telephone follow up can significantly increase recruitment levels (Treweek *et al.*, 2010; Watson & Torgerson, 2006) as have individual studies (Zaslavsky *et al.*, 2002).

5.6 Ethical Issues

5.6.1 Approval

Ethical approval was granted from the NHS Tayside Research Ethics Committee. Management approval was granted from NHS Tayside Research and Development Department and NHS Grampian Research and Development Department (see Appendix 9).

5.6.2 Confidentiality

The confidentiality of all information collected during the study was communicated to the participants in the Participant Information Sheet, the consent form and during discussion (Appendices 8 & 10). The limits to confidentiality in the event of a disclosed risk and the procedure to be followed were also highlighted in the Participant Information Sheet (see Appendix 8).

Personally identifiable data (name and date of birth) were recorded on consent forms and the data anonymising key only. All other data collected at assessment were

encoded with a unique identifier for each participant. Only the researcher and her clinical supervisor at the NHS Tayside Eating Disorder Service (EDS) had access to personally identifiable data.

5.6.3 Data Storage

Consent forms were stored in a locked filing cabinet in a locked office within a locked department on NHS Tayside property. Only the researcher and her clinical supervisor at NHS Tayside Eating Disorder Service had access to this cabinet. A key to anonymised data was stored on a password protected NHS secured memory stick which is designed to erase all data if an incorrect password is used or if it is damaged. Only the researcher had access to this password. No personally identifiable information was stored on a computer. Study related documents, such as consent forms, were transferred using personal transport.

Non identifiable data was stored in a locked filing cabinet in the same way as consent forms, but within a different NHS office. All data stored on computer was anonymised and all computers used were password protected, including a home laptop which also had anti-virus software. One NHS memory stick, as described above, was used to transfer data between sites. Data was stored in line with the Data Protection Act (Department of Health, 1998), NHS Tayside Information Governance Policy (2010) and NHS Code of Practice on Protecting Patient Confidentiality (Scottish Executive, 2003).

Following study completion, personally identifiable data will be stored for 6-12 months and then destroyed, as recommended by NHS Tayside Research and Development Office. Non-identifiable data will be stored for 5 years from the date of publication in accordance with NHS Tayside Research and Development guidance (Tayside Medical Science Centre, 2011).

5.6.4 Potential Distress to Participants/Disclosure of risk issues

There was a risk that participants may have found the questionnaires and neuropsychological testing upsetting. A number of measures were taken to address this possibility. Referring clinicians were asked to use their judgement as to the current emotional state of the patient and their ability to undergo neuropsychological testing. Then, at the beginning of the session, participants were reminded that they were free to withdraw at any time. In addition, following participation, the investigator had a general discussion with the participant about how they found the testing, providing general feedback on neuropsychological test performance and explanation of the normal range of test performance. Written feedback was available on request.

As self harm and suicidality can be a risk factor in BN, as well as a potential risk factor for patients with severe anxiety or depression, items 15 and 59 of the SCL-90-R, relating to distress caused by ‘thoughts of ending your life’ and ‘thoughts of death or dying’, were routinely checked after administration of the questionnaire and discussed with the participant if any issues of risk were highlighted. Similarly, the first two items on the YBOCS symptom checklist, ‘I fear I might harm myself’ and ‘I fear I might harm other people’ were also checked and discussed with the participant if endorsed.

In the event of the procedure causing distress or an issue of risk being disclosed, participants were able to speak to the researcher in the first instance and, if further assistance was needed, the researcher’s clinical supervisor, a Consultant Clinical Neuropsychologist, was contactable to advise on immediate and longer term care for the patient including discussing the issue with their treating clinician and/or referral to other appropriate areas of the service.

As participation in the study required approximately 1.5 to 2 hours, there was potential for the participant to become fatigued. For this reason, participants were offered a break between neuropsychological testing and questionnaire completion.

There were potential benefits for participants. Participants may have enjoyed the experience of participation in neuropsychological testing, as neuropsychological research indicates many participants do (Bennett-Levy *et al.*, 1994). They may also have felt positive about contributing to research that will increase the understanding of their condition and potentially help future patients.

5.7 Data analysis

Data were analysed using SPSS version 15.

5.7.1 Investigating assumptions for parametric statistical testing

The data was first explored using graphing, tests of normality and homogeneity of variance to confirm that it met the assumptions for appropriate use of parametric statistics.

5.7.2 Main analysis

The main aim of the study was to explore potential differences between the two groups on measures of set shifting, inhibition, psychopathology and eating pathology. A priori key measures were identified in order to reduce the number of comparisons within the data. Key measures chosen were TMT4 completion time and TMT4 number of errors, WCST Perseverative errors, WCST categories completed, WCST non-perseverative errors, Stroop Interference 3 and Hayling number of errors.

Comparisons were made using independent samples t-tests and Mann-Whitney U tests with Bonferroni corrections for multiple comparisons. When a number of comparisons are being performed on a dataset, Bonferroni's correction dictates that the alpha level should be divided by the number of comparisons. The alpha level used for this study was 0.05, however where Bonferroni's correction is applied a smaller value will be required to reach significance.

The relationship of general psychopathology and eating pathology to set shifting and inhibition was explored within groups using correlational analysis. Kendall's tau

correlations were conducted between the identified a priori set shifting and inhibition variables and the relevant psychological measures. Anxiety symptoms were described by the anxiety scale of SCL-90 and by the YBOCS score. Depressive symptoms were described by the SCL-90 depression subscale (as described in Chapter 4).

As differences between the groups on neuropsychological measures were non-significant, a post-hoc regression analysis was conducted to investigate the predictive ability of measures of anxiety, depression and obsessive-compulsive symptoms on neuropsychological performance (Chapter 4).

5.7.3 Additional Analysis

Further analysis of the data presented in Chapter 4, and analysis of measures not chosen as a priori key measures, but included in the research, are also described.

Following that, analysis related to the secondary aims of the thesis, and the measures of Social Problem Solving and Self Esteem are described.

5.7.3.1 Clinical significance of impaired performance

Clinically significant impairment in set shifting and inhibition was determined on a case by case basis by using standardised test norms.

In order to investigate clinically significant impairment, two comparisons were conducted. Each participant's performance on key measures was compared to their estimated premorbid IQ and to normative data. Z scores were calculated for the NART estimated IQ and each a priori key measure using standard scores. Underperforming was defined as the Z score of neuropsychological test performance falling one standard deviation (SD) or more below the Z score of the individual's estimated premorbid ability, indicated by NART IQ. Participants underperforming on 3 or more measures were highlighted as potentially impaired relative to past ability. Each participant's performance was also compared to the normative data for each measure using 2 SDs below the mean as a cut off point for impairment.

5.7.3.2 Secondary Variables

Further exploratory analysis of set shifting and inhibition were conducted comparing the performance of the two groups on other variables not identified as key variables but commonly reported in the literature. Secondary variables were DKEFS Letter Fluency, DKEFS Category Fluency, DKEFS Category Shift and Brixton total errors.

Self reported self esteem as measured by the SLSC and self reported social problem solving style as measured by the SPSI were also compared between groups. The relationship between social problem solving and self esteem, set shifting and inhibition was also investigated using correlational analysis in the Additional Results Chapter (Chapter 6).

5.7.4 **Missing Data**

Missing data were treated as follows:

Missing values were found in the items of both the SCL-90 and SPSI-R for two participants. These missing items were replaced by the participant's average value for the existing items on that subscale assuming that no more than 2 items were missing from a subscale. Neither questionnaire had more than 1 missing value per participant in the collected data. One BN participant failed to complete the SPSI, YBOCS or SLSC. This participant was excluded from analyses of these variables.

5.8 **Statistical Power and Sample Size**

The issue of limited power due to small sample sizes has been highlighted in many recent reviews of neuropsychological impairment in BN, as a major limitation present in most of the current research (Roberts *et al.*, 2007; Van den Eynde *et al.*, 2011). Only 13 of 37 studies included in a recent systematic review of neuropsychological impairment in BN patients, had sample sizes of 26 or greater, which is a necessary sample size to detect large effect sizes between two groups using t-tests with 80% power and a 0.05 two-tailed significance level (Van den Eynde *et al.*, 2011). Effect sizes found in comparisons between BN groups and healthy controls are reported to be large to medium (Van den Eynde *et al.*, 2011).

No studies were found that compared bulimic and anxious or depressed groups on similar measures of cognitive abilities, from which to estimate an expected effect size for the comparisons in this study. An appropriate sample size was determined by first estimating an expected effect size from the literature. Means and standard deviations for samples of people diagnosed with bulimia, anxiety and depressive disorders were obtained from existing literature, relating to the a priori key subscales of the WCST. Effect sizes were estimated using these data and subsequently appropriate sample sizes were determined using the parameters of a power of 80% and a 0.05 two-tailed significance level (using GPower 3.1.2). Difficulties related to these comparisons are reported in section 5.8.1.

Effect sizes estimated for the variable ‘categories completed’ were calculated using data from Alvarez-Moya *et al.* (2009) and Roberts *et al.* (2010) in samples of patients with BN, and from Stordal *et al.* (2004) and Merriam *et al.* (1999) in samples of patients with depressive symptoms. Effect sizes estimated from this data ranged from 0.78 to 1.2 and group size determined ranged from 12 participants per group to 27 participants per group.

Effect sizes estimated for the variable ‘perseverative errors’ were calculated using data from Galderisi *et al.* (2011) for a BN sample, from Merriam *et al.* (1999) and Stordal *et al.* (2004) for samples of patients with depressive symptoms and from Boldrini *et al.* (2005) and Abbruzzese *et al.* (1995) for samples of patients with anxiety disorders. Effect sizes estimated from this data ranged from 0.14 to 0.76 comparing samples of patients with BN to those with anxiety disorders, and from 0.806 to 1.06 comparing samples of patients with BN and depression. These effect sizes lead to proposed sample sizes of 14, 15, 21, 28, 123 and 781 participants per group.

In light of the varied sample sizes determined from the data, a maximum sample size of 40 participants was chosen for each group. A sample size of 26 was determined to be adequate to detect the large to medium effect size estimated from the literature.

5.8.1 Difficulties identifying appropriate data for use in determining sample size

Unfortunately, as has been pointed out in many review papers (Van den Eynde *et al.*, 2011; Zakzanis *et al.*, 2010), it is a limitation of the available research that tests have been chosen and results reported in such a way that direct comparisons between papers are difficult. In reviewing recent studies, it was found that even when the same test measures are used, some studies may report medians, while some report means; some report a combined or composite scores such as TMT B-A, while others report B and A separately. As such, comparison of means and standard deviations across the areas of eating disorders, anxiety disorders and depression, was only possible for some of the a priori key measures and for some patient samples in order to estimate the effect sizes to be expected in this study.

Chapter 6: Additional Results

Analyses of data relating to Aims 1 and 2 of the Thesis project are described in Chapter 4. Further analysis of these data, including the assessment of normality, is described below. Analysis of measures not chosen as a priori key measures, but included in the research are also described here. Following this, analysis related to Aim 3 of the thesis, exploring social problem solving and self esteem in the BN and AD groups is reported.

6.1 Further analysis of data presented in Chapter 4

6.1.1 Assessing Normality of the Data

The a priori variables were assessed for the assumptions of normality by examining the Z scores of skewness and kurtosis, the Shapiro-Wilkes test of normality and Levene's test of equal variance between the BN group and the AD group (see Table 6.1). Results indicated that only the variable Stroop interference, met the assumptions of normality in both groups. The variable TMT condition 4 also met the assumptions of normality but only in the BN group. All other variables analysed were assessed for normality in a similar way.

Table 6.1 Test of Normality Assumptions

	Mean (SD)	Median	Skew (SE)	Skew Z	Kurtosis (SE)	Kurtosis Z	Shapiro -Wilks	P	Levene p
WCST									
perseverative	12.45		2.22		6.20				
Errors	(9.76)	10	(.36)	6.2†	(.70)	8.8†	0.773	.001*	.045*
	10.71		1.13		1.28				
BN	(6.36)	10	(.50)	2.3†	(.97)	1.3	0.891	.023*	
	14.04		1.98		4.123				
AD	(11.96)	8	(.48)	4.1†	(.94)	4.4†	0.761	.001*	
Categories	5.06		-1.77		2.10				
completed	(1.74)	6	(.36)	5.0†	(.70)	3.0†	0.6.7	.001*	ns
	5.19		-2.14		4.14				
BN	(1.66)	6	(.50)	-4.3†	(.97)	4.3†	0.570	.001*	
	4.91		-1.61		1.52				
AD	(1.83)	6	(.48)	3.3†	(.94)	1.6	0.664	.001*	
Non-									
perseverative	15.21		2.10		4.74				
errors	(16.34)	8	(.36)	0.8	(.70)	6.8†	0.734	.001*	ns
	16.62				3.57				
BN	(20.5)	7	2.07(.50)	4.1†	(.97)	3.7†	0.677	.001*	
	13.91(1		1.00		-0.09				
AD	(1.7)	9	(.48)	2.1†	(.94)	-0.1	0.841	.002*	
	72.82		1.11		3.56				
TMT4	(24.5)	72.15	(.36)	3.1†	(.70)	5.1†	0.920	.005*	ns
	69.21		-0.20		0.95				
BN	(22.4)	73.2	(.50)	0.4	(.97)	1.0	0.962	.553	
	76.12		1.83		4.44				
AD	(26.3)	71.1	(.48)	3.8†	(.94)	4.7†	0.844	.002*	
	0.61		3.40		13.41				
TMT4 errors	(1.5)	0	(.36)	9.5†	(.70)	19.1†	0.475	.001*	.039*
	0.90		2.84		8.91				
BN	(0.43)	0	(.50)	5.7†	(.97)	9.2†	0.545	.001*	
	0.35		3.23		11.11				
AD	(0.93)	0	(.48)	6.7†	(.94)	11.9†	0.442	.001*	
Stroop	49.67		0.78		1.24				
interference	(12.8)	47.95	(.36)	2.2†	(.70)	1.8	0.960	.126	ns
	47.06		0.30		0.93				
BN	(2.33)	46.1	(.50)	0.6	(.97)	1.0	0.965	.618	
	52.05(1		0.79		1.35				
AD	(4.31)	49.4	(.48)	1.6	(.94)	1.4	0.953	.334	
	1.73		3.64		15.75				
Hayling errors	(3.22)	1	(.36)	10.2†	(.70)	22.4†	0.555	.001*	ns
	1.05		2.61		7.70				
BN	(1.69)	1	(.50)	5.2†	(.97)	7.9†	0.644	.001*	
	2.35		3.02		10.1				
AD	(4.10)	1	(.48)	6.3†	(.94)	10.8†	0.595	.001*	

ns = non-significant, Z = value/SE,

†= values not consistent with assumptions of normality

6.1.2 Further details on analysis of Age normed scaled scores for a priori variables

As described in Chapter 4, the BN group was significantly younger than the AD group. Therefore, differences between the groups on age normed scaled scores were investigated on neuropsychological measures, where such scaled scores were available. These data were non-normal for all but CWIT inhibition, therefore Mann Whitney U tests were used in the majority of comparisons. Further detail of these comparisons is provided here.

WCST perseverative errors scaled scores (SS) did not differ significantly between the BN group (Mdn=97) and the AD group (Mdn=96), $U=202.5$, $Z=-.918$, ns, $r=-0.14$. The BN group (Mdn=10) also did not differ significantly from the AD group (Mdn=11) on TMT condition 4 scaled scores, $U=205.5$, $Z=-.857$, ns, $r=-.13$. Differences between the BN group ($M=11.24$, $SD=2.68$) and the AD group ($M=10.74$, $SD=3.25$) were non-significant on CWIT inhibition, $t(42)=0.552$, $p=.584$, $r=.007$, and on CWIT inhibition switch (BN median =12, AD median = 11), $U=173$, $Z=-1.62$, ns, $r=-.25$. These results still indicate the non-significant effects seen when using non age corrected variables.

6.1.3 Relationship of general and eating psychopathology

A number of associations between general psychopathology and eating disorder psychopathology were seen in the BN group. A significance level of $p < .01$ was chosen, as a Bonferroni correction was considered too conservative for this analysis. Increased Eating Restraint was associated with increased depression among BN participants. Increased Restraint was also associated with increased distress on the 'Additional' subscale of the SCL-90-R, which contains items related to sleep and appetite disturbance. Increased Eating Concern was significantly associated with obsessive-compulsive symptoms as measured by the SCL-90-R but not by the YBOCS, and with higher distress on the 'Additional' scale. Weight concern was significantly associated with increased scores on the 'Additional' scale and the Positive Syndrome Distress Index. Only Shape Concern was not significantly associated with increased psychological symptoms, at the $p < .01$ level.

Table 6.2 Correlation of general and eating psychopathology in BN group

	YBOCS		EDE		
		<i>Restraint</i>	<i>Eating</i>	<i>Shape</i>	<i>Weight</i>
SCL-90					
O-C	.114	.272	.459**	.332*	.403*
Depression	-.011	.426**	.390*	.254	.364*
Anxiety	.255	.301	.355*	.365*	.294
Phobia	.158	.230	.156	.212	.412*
Somatisation	.216	.252	.297	.350*	.284
Hostility	.001	-.106	.139	.095	.075
I-S	.124	.103	.189	.005	.137
Paranoia	-.033	-.025	.168	.069	-.030
Psychoticism	.361*	.139	.284	.275	.257
Additional	.102	.457**	.475**	.295	.537**
GSI	.208	.307	.388*	.360*	.377*
PSDI	.117	.272	.373*	.402*	.419**
Y-BOCS	1.000	.038	.160	.096	-.043

O-C = obsessive-compulsive scale, I-S = interpersonal sensitivity

* $p < .05$, ** $p < .01$, PSDI=Positive Syndrome distress index, GSI = Global Severity Index

In the AD group, there was only one significant relationship between eating pathology and general pathology. Increased Eating Restraint was associated with lower Phobic anxiety as measured by the SCL-90-R, however this did not appear to be a true trend in the data after inspection of graphs (see Appendix 11).

Table 6.3 Correlation of general and eating psychopathology in AD group

	YBOCS	EDE			
		<i>Restraint</i>	<i>Eating</i>	<i>Shape</i>	<i>Weight</i>
SCL-90					
O-C	.213	-.089	.270	.242	-.033
Depression	.202	-.249	.168	.231	-.041
Anxiety	.225	-.355*	.099	.065	-.221
Phobia	.118	-.538**	-.110	.095	-.156
Somatisation	-.021	-.265	-.113	.004	-.195
Hostility	.258	-.037	.156	.267	.026
I-S	.212	-.222	.137	.270	-.013
Paranoia	.181	-.101	.142	.212	.199
Psychoticism	.358*	-.189	.311	.348*	.001
Additional	.256	-.185	.197	.228	-.083
GSI	.290	-.288	.185	.237	-.082
PSDI	.274	-.244	.204	.261	-.057
Y-BOCS	1	.045	.125	.207	-.106

O-C = obsessive-compulsive scale, I-S = interpersonal sensitivity

* $p < .05$, ** $p < .01$, PSDI=Positive Syndrome distress index, GSI = Global Severity Index

6.1.4 Clinically Significant Impairment

17 patients (81%) from the BN group and 18 (78%) from the AD group performed at least 1 standard deviation (SD) below their estimated premorbid ability on one or more a priori measure. Underperformance relative to estimated premorbid ability on 3 or more measures was defined as impaired, relative to estimated premorbid ability. Seven from the BN group and 12 from the AD group demonstrated underperformance on 3 or more measures (Table 6.4).

Impaired performance relative to normative data was defined as performance at 2 SDs or more below the normative mean on one or more measures. Five people from the AD group and 3 from the BN group were impaired relative to normative data. These participants were also impaired relative to past ability.

The measures on which the underperformance and impaired performance occurred are described in Table 6.4.

Table 6.4: Number of participants demonstrating underperformance and impairment

	Underperformance on at least 1 measure (%)		Underperformance on 3 or more measures (%)		Impaired relative to normative group on 1 or more measure (%)	
	<i>BN</i>	<i>Anx/Dep</i>	<i>BN</i>	<i>Anx/Dep</i>	<i>BN</i>	<i>Anx/Dep</i>
<u>Set Shifting</u>						
WCST						
Perseverative errors	9 (43)	14 (61)	7 (33)	11 (48)	0	1 (4)
Categories completed	10 (48)	13 (57)	7 (33)	12 (52)	2 (10)	1 (4)
DKEFS						
Trail Making test						
Number/letter switch	6 (29)	3 (13)	3 (14)	2 (9)	0	1 (4)
Trail Making test						
Number of errors	2 (10)	4 (17)	2 (10)	4 (17)	0	1 (4)
<u>Inhibition</u>						
WCST						
Non-perseverative errors	11 (52)	14 (61)	7 (33)	12 (52)	3 (14)	2 (9)
Colour Word						
Inhibition	4 (19)	6 (26)	2 (10)	4 (17)	0	1 (4)
Hayling						
Errors	1 (5)	2 (9)	1 (5)	2 (9)	0	1 (4)
Total Number of individuals	17 (81)	18 (78)	7 (33)	12 (52)	3 (14)	5 (22)

Those defined as impaired relative to past ability were significantly younger than unimpaired participants ($U=119.5$, $Z=-2.799$, $p < .05$), scored lower on EDE restraint ($U= 126$, $Z = -2.657$, $p < .05$), had higher estimated premorbid IQ ($t(42) = 3.82$, $p < .05$) and scored lower on the YBOCS ($t(442) = 2.42$, $p < .05$). There was no difference in BMI, years of education or SCL-90-R subscales anxiety, depression or obsessive compulsive symptoms.

Individuals from either group with a deficit relative to normative data were not significantly different to the rest of the participants (all $p>.05$) on age, BMI, premorbid IQ, years of education, EDE restraint, SCL-90-R subscales of anxiety, depression, obsessive compulsive symptoms or the YBOCS.

The proportions of each group who were impaired relative to normative data ($p = .701$; FET) or relative to previous ability ($p = .239$; FET) were not significantly different.

6.1.5 Relationships between performance on different neuropsychological measures

In the BN group, there were no significant correlations of set shifting measures with each other after a correction for multiple comparisons of $p < .01$ was applied, although increased perseverative errors were associated with fewer categories completed, at the level of $p < .05$. However, non-perseverative errors were significantly correlated with categories completed, indicating that increased non perseverative errors was strongly related to fewer categories being completed by BN participants. No significant correlations were found between the inhibition measures, suggesting that participants in the BN group did not perform in a similar way on all the inhibition measures (Table 6.5).

Table 6.5 Relationship between performance on set shifting and inhibition measures in the BN group

	WCST		DKEFS TMT		WCST	CWIT	Hayling
	PE	CC	N/L switch	Errors	NPE	Inhibition	Errors
Set Shifting							
WCST							
Perseverative errors (PE)		-.467*	.138	.255	.632*	-.128	-.101
Categories completed (CC)	-.467*		.037	-.084	-.646**	.373*	.195
DKEFS							
Trail Making test							
Number/letter switch	.138	.037		.247	.170	.329*	.093
Trail Making test No. of errors	.255	-.084	.247		.132	-.041	-.414*
Inhibition							
WCST							
Non-perseverative errors (NPE)	.632*	-.646**	.170	.132		-.077	-.076
DKEFS							
Colour Word Inhibition	-.128	.373*	.329*	-.041	-.077		.237
Hayling Errors	-.101	.195	.093	-.414*	-.076	.237	

* $p < .05$, ** $p < .01$

In the AD group, there were no significant correlations between measures of inhibition. However, a trend was seen relating increased WCST non-perseverative errors with longer times to complete the CWIT inhibition condition. Measures of set shifting tended to be significantly correlated with each other in the AD group,

indicating that participants who performed poorly on one set shifting task also showed impairment across the others. However, the number of errors on TMT number/letter switch was not correlated with other set shifting measures, which suggests that it may not reflect the same difficulties as the other set shifting measures.

There were also significant correlations between inhibition and set shifting measures, as increased non-perseverative errors were associated with increased time to complete the TMT number/letter switch task and increased perseverative errors. This indicates that participants who performed poorly on set shifting tasks also committed more non-perseverative errors, suggesting that their cognitive inhibition was also impaired.

Unlike the BN group, correlations within the AD group indicate that both perseverative and non-perseverative errors contributed approximately the same amount to impaired category completion among AD participants (Table 6.6).

Table 6.6 Relationship between performance on set shifting and inhibition measures in the anxious and/or depressed group

	WCST		DKEFS TMT		WCST	CWIT	Hayling
	PE	CC	N/L switch	Errors	NPE	Inhibition	Errors
<u>Set Shifting</u>							
WCST		-.666**	.490**	.208	.717**		
Perseverative errors (PE)						.288	.163
Categories completed (CC)	-.666**		-.447**	-.147	-.691**	-.312	-.215
DKEFS							
Trail Making test	.490**	-.447**		.286	.435**		
Number/letter switch						.217	.212
Trail Making test No. of errors	.208	-.147	.286		.151	.314	.149
<u>Inhibition</u>							
WCST	.717**	-.691**	.435**	.151			
Non-perseverative errors (NPE)						.346*	.168
DKEFS	.288	-.312	.217	.314	.346*		
Colour Word Inhibition							.071
Hayling Errors	.163	-.215	.212	.149	.168	.071	

* $p < .05$, ** $p < .01$

6.2 Non-key Executive function measures and additional subscales of the SCL-90-R

The groups were compared on the Brixton task and the three conditions of the DKEFS Verbal Fluency task, which formed part of the neuropsychological battery, but were not chosen as a priori measures. No significant differences were observed between the groups on the Brixton task or the three tasks of Verbal Fluency. Similar levels of psychopathology symptoms, on the paranoia, psychoticism and ‘additional’ subscales of the SCL-90-R were also seen in the two groups (Table 6.7).

6.3 Analysis Relating to Aim 3 - Social Problem Solving and Self Esteem

The self esteem and social problem solving styles of the BN and AD participants were investigated using the Self-Liking/Self Competence scale (SLSC) and the Social Problem Solving Inventory (SPSI).

6.3.1 Social Problem Solving Style

The dimensions identified by the Social Problem Solving Inventory are Positive Problem Orientation (PPO), Negative Problem Orientation (NPO), Rational Problem Solving (RPS), Impulsivity/Carelessness style (ICS) and Avoidance style (AS). Adaptive social problem solving is indicated by the subscales PPO and RPS. Maladaptive problem solving is indicated by subscales NPO, ICS, AS. The SPSI provides standard scores for each dimension of social problem solving with a mean of 100 and a standard deviation of 15.

Both groups obtained mean scores one standard deviation lower than the normative group on PPO and one standard deviation higher than the normative group in NPO, indicating maladaptive problem orientation in both groups (Figures 6.1 and 6.2).

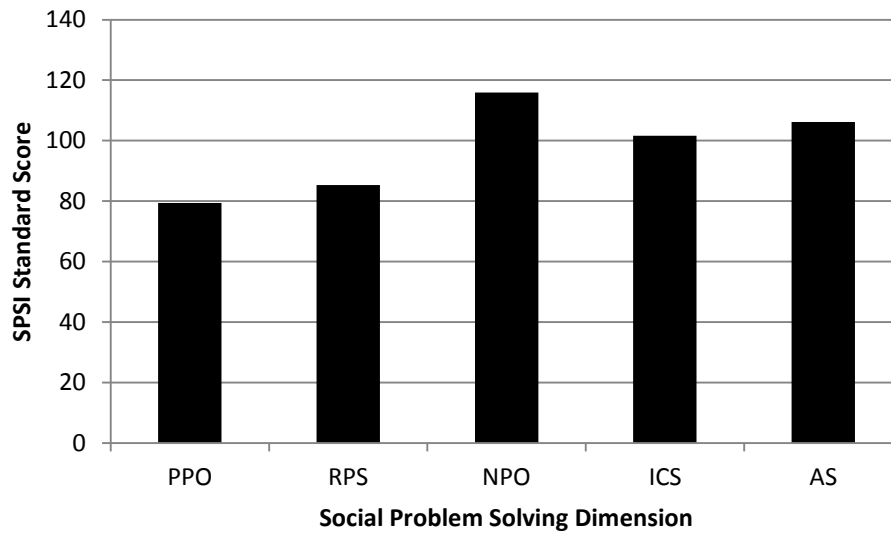


Figure 6.1 Social Problem Solving Styles of the BN group

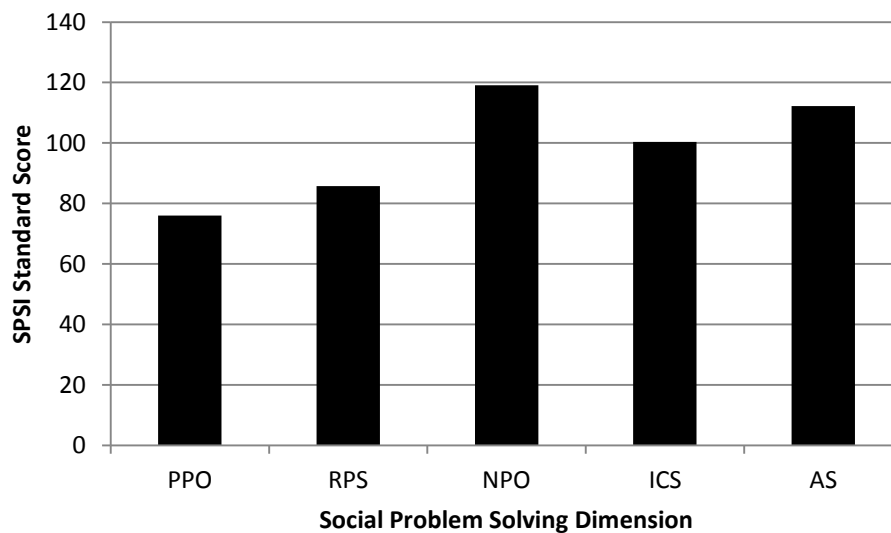


Figure 6.2 Social Problem Solving Styles of the AD group

6.3.2 Group comparisons of self esteem and social problem solving

As all the variables were found to be normally distributed, t-tests were used to compare groups. The age standardised scores for the SPSI were used for the comparison as the two groups had been found to differ significantly on age (Chapter 4).

The BN group indicated significantly lower self liking and sense of self competence than the anxious/depressed group, illustrated on the total score of the Self Liking/Self Competence scale ($t(41)=-2.824, p < .01$) and on its individual scales, Self liking ($t(41)=-2.674, p < .05$) and Self competence ($t(41)=-2.417, p < .05$). The two groups demonstrated no significant differences in social problems solving styles (Table 6.7).

Table 6.7: Comparison of groups on additional psychological variables and non key executive function measures

	Bulimic group n=21			Anxiety/Depression group n=23			Cohen's				
	<i>Mean</i>	<i>SD</i>	<i>Median (range)</i>	<i>Mean</i>	<i>SD</i>	<i>Median (range)</i>	<i>t</i>	<i>U</i>	<i>p</i>	<i>d</i>	<i>r</i>
<u>Psychological Variables</u>											
SCL-90-R (PSDI)	2.35	0.71		2.12	.60		1.16		.254	0.35	
Paranoia	6.81	6.87	5 (0-25)	4.91	3.82	5 (0-13)		212	.493		-0.11
Psychoticism	6.52	5.87	5 (0-21)	6.39	5.65	5 (0-20)		234.5	.875		-0.02
Additional	12.52	6.97		9.48	5.62		1.60		.117	0.48	
<u>SPSI-R^a</u>											
PPO	79.35	18.93		75.96	15.59		0.645		.523	0.20	
NPO	115.95	18.20		119.09	19.41		0.544		.589	-0.17	
RPS	85.3	12.17		85.74	13.63		0.111		.912	-0.03	
I-CS	101.65	14.21		100.30	11.86		0.338		.737	0.10	
Avoidance style	106.20	15.28		112.22	13.58		1.367		.179	-0.42	
Global Score	87.55	17.62		81.74	13.41		1.226		.227	0.37	
<u>SLSC^a</u>											
Self liking	15.25	4.89		19.30	5.01		2.674		.011*	-0.82	
Self Competence	17.55	6.18		21.6	4.82		2.417		.020*	-0.73	
Total Score	32.8	9.75		40.9	9.08		2.824		.007**	-0.86	
<u>Neuropsychological Variables</u>											
<u>DKEFS Verbal Fluency</u>											
Letter Fluency	42.71	10.12		39.48	12.51		0.94		.354	0.28	
Category Fluency	45.19	7.96		41.65	8.94		1.38		.175	0.42	
Category Shift, total switching acc	14.33	3.69		13.78	3.04		0.54		.591	0.16	
Brixton errors	12.62	3.35		21.57	34.90		1.17		.249	-0.36	

a one participant failed to complete the SPSI-R and the SLSC, therefore n=20 in the BN group on these measures

**p*<.05, ** *p*<.01, PSDI=Positive Syndrome distress index

6.3.3 Relationship between a priori variables and Social Problem Solving

A significance level of $p < .01$ was chosen, as a Bonferroni correction was considered too conservative for the analysis. Social problem solving was not significantly related to any of the neuropsychological measures in the BN group (Table 6.8).

Table 6.8: Correlation of Social Problem Solving Patterns and a priori variables in the BN group

	Adaptive Problem Solving		Maladaptive Problem Solving		
	<i>PPO</i>	<i>RPS</i>	<i>NPO</i>	<i>ICS</i>	<i>AS</i>
<u>Set Shifting</u>					
WCST					
Perseverative errors	.134	-.066	-.060	-.245	-.045
Categories completed	.057	.073	.136	.244	-.008
DKEFS					
Trail Making test					
Number/letter switch	.114	-.199	.001	-.157	-.098
Trail Making test No. of errors	.099	-.212	.270	-.183	-.122
<u>Inhibition</u>					
WCST					
Non-perseverative errors	.077	.055	-.022	-.154	.083
DKEFS					
Colour Word Inhibition	.097	.097	.059	.130	.070
Hayling Errors	-.026	.033	-.265	.131	.053

* $p < .05$, ** $p < .01$ PPO = Positive Problem Orientation, RPS = Rational Problem Solving, NPO = Negative Problem Orientation, ICS = Impulsivity/Carelessness Style, AS = Avoidance Style

Within the AD group, trends of association were seen that were not significant at the chosen $p < .01$ level. There was a trend of association between NPO and WCST categories completed and between Impulsivity/Carelessness style and errors on the Hayling task. Endorsement of rational problem solving strategies showed a trend of association with fewer errors on the TMT. Upon visual inspection of graphs, there were no visible trends in the data (see graphs in Appendix 11).

Table 6.9 Correlation of Social Problem Solving Patterns and a priori variables in the AD group

	Adaptive Problem Solving		Maladaptive Problem Solving		
	<i>PPO</i>	<i>RPS</i>	<i>NPO</i>	<i>ICS</i>	<i>AS</i>
<u>Set Shifting</u>					
WCST					
Perseverative errors	.137	-.176	-.099	-.107	.055
Categories completed	-.134	.152	.364*	-.058	-.108
DKEFS					
Trail Making test					
Number/letter switch	.238	-.171	-.144	-.069	.001
Trail Making test No. of errors	.303	-.401*	.241	-.057	-.318
<u>Inhibition</u>					
WCST					
Non-perseverative errors	.127	-.143	-.074	-.075	-.051
DKEFS					
Colour Word Inhibition	-.040	-.020	.120	.012	-.065
Hayling Errors	.222	-.062	-.085	.320*	-.005

* $p < .05$, ** $p < .01$ PPO = Positive Problem Orientation, RPS = Rational Problem Solving, NPO = Negative Problem Orientation, ICS = Impulsivity/Carelessness Style, AS = Avoidance Style

6.3.4 Relationship between a priori variables and Self-Liking and Self-Competence

No relationships were found between reported self liking or self competence and performance on the set shifting and inhibition measures in either group (Table 6.10).

Table 6.10: Association between a priori variables and self liking/self competence

	BN Group			AD Group		
	<i>SL</i>	<i>SC</i>	<i>Tot</i>	<i>SL</i>	<i>SC</i>	<i>Tot</i>
<u>Set Shifting</u>						
WCST						
Perseverative errors	.184	.172	.160	.185	.128	.188
Categories completed	-.049	.049	.072	-.287	-.213	-.273
DKEFS						
Trail Making test						
Number/letter switch	.309	.292	.284	.279	.283	.295
Trail Making test No. of errors	.114	.303	.271	.182	.143	.219
<u>Inhibition</u>						
WCST						
Non-perseverative errors	.176	.038	.033	.131	.046	.123
DKEFS						
Colour Word Inhibition	.249	-.005	.086	.033	-.057	-.008
Hayling Errors	.171	.013	.071	-.014	.050	.001

* $p < .05$, ** $p < .01$, SL = Self Liking, SC = Self Competence, Tot = Self Liking/Self Competence total score

Chapter 7: Additional Discussion

Further analysis was performed on the data presented in Chapter 4 and data relating to two additional measures of set shifting and measures of self esteem and social problem solving were analysed in Chapter 6. The findings of these analyses will now be discussed in the order they were presented in Chapter 6.

7.1 Age differences between groups

Participants in the BN group were significantly younger than patients in the AD group. This difference was most likely related to the fact that the average age of onset of bulimia (20yrs) is younger than average onset of depression (30yrs), GAD (31 yrs) or Panic Disorder (24yrs) although not of OCD (19yrs) (Hudson *et al.*, 2007; Kessler *et al.*, 2005). As such, these age differences are likely to represent inherent characteristics of the two groups. An analysis of key variables using age normed scaled scores revealed a similar pattern of results to those using raw scores, suggesting that age did not influence the pattern of results.

7.2 Relationships of general and eating pathology

In the BN group, there were a number of correlations indicating significant relationships between eating disorder symptoms and psychopathology. This is consistent with the literature reporting a high level of comorbidity between BN and other disorders (Hudson *et al.*, 2007) and associations found in the literature such as Herpertz-Dahlmann and Remschmidt's (1993) report of a high correlation between depression and eating disorder symptoms.

In the AD group, there was no significant relationship between eating pathology and general pathology. This is to be expected, as the AD group were chosen to be without problematic levels of eating disorder symptoms ($EDE < 4$).

7.3 Clinically significant impairment

Clinical significance calculations indicated that very few participants in each group were impaired on any neuropsychological test compared to normative data. Similar proportions of participants in each group underperformed and demonstrated impairments in relation to normative data. Overall, the performance of each group was relatively unimpaired compared to normative data, although a high proportion of

participants were underperforming relative to their own estimated premorbid ability. This is consistent with many findings of no impairments relative to controls in studies of BN, anxiety and depression on executive function tasks (Brand *et al.*, 2007; Claes *et al.*, 2006; McClintock *et al.*, 2010). Most participants in the AD group used here were diagnosed with GAD, specific phobia or panic disorder with or without comorbid depression. The literature would suggest that a group of this composition would not have specific deficits in set shifting or inhibition (Airaksinen *et al.*, 2005; Chapter 2 of this thesis; O'Toole & Pedersen, 2011). Findings of relatively few participants who were significantly impaired among a sample of eating disorder patients is consistent with the literature. Approximate proportions of 65% unimpaired and 35% impaired were reported by Lauer *et al.* (1999) in relation to their own study of BN and AN and in their discussion of other eating disorder studies (Kingston *et al.*, 1996).

When considering performance among the impaired participants, different patterns were seen. Participants in the AD group were impaired across all a priori measures, while BN participants were exclusively impaired on WCST non-perseverative errors (NPE) and number of categories completed (CC). A pattern similar to this in BN participants was reported by Alvarez-Moya *et al.* (2009), where BN participants made significantly more non-perseverative errors than healthy controls. Barceló and Knight (2002) have suggested that WCST NPE can reflect random errors relating to impairments in maintaining set, due to distractibility or impulsivity. In their sample of patients with prefrontal lobe injuries, the CC score, which is often taken to relate to set shifting errors, was in fact more commonly lowered due to failure to continue with a correct responding pattern. This implies that where NPE is impaired, impaired CC may not indicate set shifting difficulties but is rather a consequence of the high number of NPEs. There is a 'failure to maintain set' scale in the WCST, which measures a similar construct, but this only counts errors after five or more correct matches. NPE may reflect shorter durations of set-consistent responding. Although these impairments suggest the presence of cognitive disinhibition, similar impairments relative to normative data were not seen on the other measures of inhibition, i.e. the Stroop inhibition task and the Hayling task.

7.4 Relationships between performance on neuropsychological measures

Set shifting measures correlated with each other in the AD group but not in the BN group. This analysis suggests (in addition to the clinical impairment analysis) that despite non-significant differences between groups, the style of performance was different in each group.

In the BN group, there were no significant correlations of set shifting measures with each other, after a correction for multiple comparisons, nor were inhibition measures correlated with each other. However, non-perseverative errors were significantly correlated with categories completed. This indicates that increased non perseverative errors were strongly related to fewer categories being completed by BN participants, and supports the idea that a low number of categories completed is related to loss of set, rather than perseverative set maintenance, in this group.

In the AD group, there were no significant correlations between measures of inhibition, suggesting that AD participants performed differently on each measure of inhibition. Measures of set shifting tended to be significantly correlated with each other, suggesting that participants who performed poorly on one set shifting task also displayed impairment across other set shifting tasks. However, the number of errors on TMT number/letter switch task was not correlated with the other set shifting measures, which suggests that participants in the AD group did not perform on it in the same way as they did on the other set shifting measures. Many neuropsychological measures can be said to assess a number of cognitive functions (Burgess, 2003). In this case, the number of errors on the TMT number/letter switch task may not have been primarily tapping into the same ability as the other set shifting tasks in the AD group.

There were significant correlations between inhibition and set shifting measures in the AD group, as increased non-perseverative errors were associated with increased time to complete the TMT number/letter switch task. This suggests that participants who performed poorly on set shifting tasks also committed more non-perseverative errors and indicates that patients with set shifting impairments in this group may also have been impaired in cognitive inhibition.

Unlike the BN group, where only NPE made a significant contribution to the categories completed variable in the WCST, in the AD group both perseverative and non-perseverative errors contributed approximately the same amount to impaired category completion.

7.5 Non-key Executive Function Measures

No group differences were found on the additional measures of verbal fluency and set shifting, which is consistent with the lack of group differences on set shifting measures reported in Chapter 4. It is also consistent with literature that indicates that the performance of BN patients on the FAS task is not different to controls (Brand *et al.*, 2007; Tchanturia, Anderluh, *et al.*, 2004).

7.6 Aim 3 – Social Problem Solving and Self Liking/Self Competence

Both groups were found to have social problem solving styles characterised by low positive problem orientation and high negative problem orientation. This similarity is consistent with the literature which suggests that BN participants would display high negative problem orientation (NPO) (Paterson *et al.*, 2011), and that high NPO has also been associated with depression (Klein *et al.*, 2011) and high levels of worry (Belzer *et al.*, 2002). These findings suggest that maladaptive social problem solving is not specific to BN and may be related to other shared factors such as anxiety and depression symptoms.

No significant differences were found in social problem solving style between the two groups. Social problem solving style was also not related to neuropsychological task performance among BN participants or AD participants.

Self esteem, as measured by the Self Liking/Self Competence scale was significantly lower in the BN group than in the comparison group of females with anxiety and/or depressive disorders. This is consistent with reports in the literature of low self-liking and self competence in AN groups relative to healthy controls (Paterson *et al.*, 2011; Paterson *et al.*, 2007). It is not consistent with similar reports of low self esteem in anxiety and depression (Silverstone & Salsali, 2003). However, neither self-liking nor sense of self competence was significantly associated with

performance on set shifting or inhibition tasks in either group. At the time of writing, no literature could be found that explored this association. However, the literature on self liking and self competence suggests that self competence is associated with perfectionism in AN (Gordon *et al.*, 2005; Surgenor *et al.*, 2007), and as perfectionism is associated with impaired set shifting (Egan *et al.*, 2011; Tchanturia, Morris, *et al.*, 2004), some relationship may have been expected between self-competence and set shifting performance. However, as has been demonstrated in a number of studies, AN and BN do not perform in the same way on neuropsychological measures (Murphy *et al.*, 2004; Roberts *et al.*, 2010), so these findings for AN may not be applicable in a BN group.

Fairburn *et al.*'s (2003) cognitive behavioural model of BN includes severe perfectionism, core low self esteem, mood intolerance and interpersonal difficulties as maintenance mechanisms for the disorder. In relation to this model of BN, these data demonstrate evidence for three of these maintaining factors. Participants in the BN group demonstrated significantly lower self esteem than a comparison group suffering from psychological distress. Perfectionism, in the form of obsessive compulsive traits, may be present at a higher level in the BN group as trends were seen (Chapter 4), however they were not found to be significant. Interpersonal difficulties also showed a trend towards being increased in the BN group on the interpersonal sensitivity scale of the SCL-90-R and the BN group demonstrated higher negative problem orientation and lower positive problem orientation than the normative group on the SPSI.

7.7 Limitations

Limitations were described in the journal article in Chapter 4.

7.8 Implications and future directions

In AN, set shifting impairments have been found to impact on Cognitive Behavioural Therapy (CBT) treatment. Cognitive remediation therapy has been used to improve cognitive flexibility and facilitate the implementation of CBT strategies with patients with anorexia (Tchanturia *et al.*, 2008). In light of the suggestion that BN participants' impairment on WCST categories completed may not relate to set shifting and in view of the small numbers demonstrating impairment, these data do

not support a need for cognitive remediation in most cases of BN. The trends relating to deficits in WCST non-perseverative errors suggest cognitive impulsivity may be a significant problem for a proportion of people with BN and as such, this study supports the possible use of some form of cognitive control training in the treatment of BN, as proposed by Robinson et al. (2009).

The finding of small proportions of a BN group demonstrating neuropsychological impairments has been seen in other studies (Lauer *et al.*, 1999) and suggests that future research may best utilise large sample sizes to investigate this small proportion of the BN population and any characteristics that may define them. Larger sample sizes would also facilitate investigation of small to medium differences that may exist between BN groups and groups representing disorders commonly comorbid with BN.

7.9 Conclusion

Eating pathology was related to anxiety and depression symptoms in the BN group but not the AD group. Further analysis indicated that few participants in either group were impaired in relation to normative data on neuropsychological measures. This evidence suggests that cognitive performance difficulties are not widespread in BN or related to anxiety, depression or obsessive compulsive symptoms. There was some tentative indication of a deficit in inhibition but this requires further investigation.

Chapter 8: References

- Abbass, A., & Mohammad, N. (2008). A comparison of social problem solving in patients with ocd, ptsd, pd and non-patient controls: To control of the intolerance of uncertainty. *Research Journal of Biological Sciences*(7), 683.
- Abbruzzese, M., Ferri, S., & Scarone, S. (1995). Wisconsin card sorting test performance in obsessive-compulsive disorder: No evidence for involvement of dorsolateral prefrontal cortex. [doi: 10.1016/0165-1781(95)02670-R]. *Psychiatry Research*, 58(1), 37-43.
- Ackard, D. M., Fulkerson, J. A., & Neumark-Sztainer, D. (2011). Psychological and behavioral risk profiles as they relate to eating disorder diagnoses and symptomatology among a school-based sample of youth. *International Journal of Eating Disorders*, 44(5), 440-446.
- Agras, W., Walsh, B., Fairburn, C. G., Wilson, G., & Kraemer, H. C. (2000). A multicenter comparison of cognitive-behavioral therapy and interpersonal psychotherapy for bulimia nervosa. *Archives of General Psychiatry*, 57(5), 459-466.
- Airaksinen, E., Larsson, M., & Forsell, Y. (2005). Neuropsychological functions in anxiety disorders in population-based samples: Evidence of episodic memory dysfunction. [doi: 10.1016/j.jpsychires.2004.06.001]. *Journal of Psychiatric Research*, 39(2), 207-214.
- Alvarez-Moya, E. M., Jiménez-Murcia, S., Moragas, L., Gómez-Peña, M., Aymamí, M. N., Ochoa, C., et al. (2009). Executive functioning among female pathological gambling and bulimia nervosa patients: Preliminary findings. *Journal Of The International Neuropsychological Society: JINS*, 15(2), 302-306.
- American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders: Dsm-iv-tr, 4th edition, text revision*. Washington, DC: American Psychiatric Press, Inc.
- Andres, P., & Van der Linden, M. (2000). Age-related differences in supervisory attentional system functions. *Journal of Gerontology: Psychological Sciences*, 55, 373-380.
- Asmundson, G. J., Stein, M. B., Larsen, D. K., & Walker, J. R. (1994). Neurocognitive function in panic disorder and social phobia patients. *Anxiety*, 1(5), 201-207.
- Axelrod, B., Goldman, R., & Woodard, J. (1992). Interrater reliability in scoring the wisconsin card sorting test. *The Clinical Neuropsychologist*, 6(2), 143.
- Baer, L. (1991). *Getting control: Overcoming your obsessions and compulsions*. London: Plume Publishing.
- Baillie, A. J., & Rapee, R. M. (2005). Panic attacks as risk markers for mental disorders*. *Social Psychiatry and Psychiatric Epidemiology*, 40(3), 240-244.
- Bannon, S., Gonsalvez, C. J., Croft, R. J., & Boyce, P. M. (2006). Executive functions in obsessive-compulsive disorder: State or trait deficits? *Australian And New Zealand Journal Of Psychiatry*, 40(11-12), 1031-1038.
- Bara-Carril, N., Williams, C. J., Pombo-Carril, M. G., Reid, Y., Murray, K., Aubin, S., et al. (2004). A preliminary investigation into the feasibility and efficacy of a cd-rom-based cognitive-behavioral self-help intervention for bulimia nervosa. *The International Journal Of Eating Disorders*, 35(4), 538-548.

- Barceló, F., & Knight, R. T. (2002). Both random and perseverative errors underlie worst deficits in prefrontal patients. [doi: 10.1016/S0028-3932(01)00110-5]. *Neuropsychologia*, 40(3), 349-356.
- Basso, M. R., Lowery, N., Ghormley, C., Combs, D., Purdie, R., Neel, J., et al. (2007). Comorbid anxiety corresponds with neuropsychological dysfunction in unipolar depression. [doi: 10.1080/13546800701446517]. *Cognitive Neuropsychiatry*, 12(5), 437-456.
- Bech, P., Allerup, P., Maier, W., Albus, M., Lavori, P., & Ayuso, J. L. (1992). The hamilton scales and the hopkins symptom checklist (SCL-90). A cross-national validity study in patients with panic disorders. *The British Journal of Psychiatry*, 160(2), 206-211.
- Bechara, A., Damasio, A. R., Damasio, H., & Anderson, S. W. (1994). Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition*, 50, 7-15.
- Beck, A. T., & Clark, D. A. (1997). An information processing model of anxiety: Automatic and strategic processes. *Behaviour Research and Therapy*, 35, 49-58.
- Belzer, K. D., D'Zurilla, T. J., & Maydeu-Olivares, A. (2002). Social problem solving and trait anxiety as predictors of worry in a college student population. *Personality and Individual Differences*, 33(4), 573-585.
- Bennett-Levy, J., Klein-Boonschate, M. A., Batchelor, J., McCarter, R., & Walton, N. (1994). Encounters with anna thompson: The consumer's experience of neuropsychological assessment. [doi: 10.1080/13854049408401559]. *Clinical Neuropsychologist*, 8(2), 219-238.
- Benton, A. L. (1945). A visual retention test for clinical use. *Archives of Neurology And Psychiatry*, 54(3), 212-216.
- Benton, A. L. (1983). *Contributions to neuropsychological assessment*. New York: Oxford University Press.
- Benton, A. L. (1989). *Multilingual aphasia examinations*. Iowa City, IA: AJA Associates.
- Berch, D. (1998). The corsi block-tapping task: Methodological and theoretical considerations. *Brain and Cognition*, 38, 317-338.
- Beumont, P. J., Kopec-Schrader, E., & Touyz, S. W. (1995). Defining subgroups of dieting disorder patients by means of the eating disorders examination (ede). *The British Journal Of Psychiatry: The Journal Of Mental Science*, 166(4), 472-474.
- Beumont, P. J., Kopec-Schrader, E. M., Talbot, P., & Touyz, S. W. (1993). Measuring the specific psychopathology of eating disorder patients. *Australian and New Zealand Journal of Psychiatry*, 27(3), 506-511.
- Bezeau, S., & Graves, R. (2001). Statistical power and effect sizes of clinical neuropsychology research. *Journal Of Clinical And Experimental Neuropsychology*, 23(3), 399-406.
- Bisaga, A., Katz, J. L., Antonini, A., Wright, C. E., Margouleff, C., Gorman, J. M., et al. (1998). Cerebral glucose metabolism in women with panic disorder. *American Journal Of Psychiatry*, 155(9), 1178-1183.
- Bjelland, I., Dahl, A. A., Haug, T. T., & Neckelmann, D. (2002). The validity of the hospital anxiety and depression scale - an updated literature review. *Journal Of Psychosomatic Research*, 52(2), 69-77.

- Black, C. M. D., & Wilson, G. T. (1996). Assessment of eating disorders: Interview versus questionnaire. *International Journal of Eating Disorders*, 20(1), 43-50.
- Boldrini, M., del Pace, L., Placidi, G., Keilp, J., Ellis, S., Signori, S., et al. (2005). Selective cognitive deficits in obsessive-compulsive disorder compared to panic disorder with agoraphobia. *Acta Psychiatrica Scandinavica*, 111(2), 150-158.
- Boleloucky, Z., & Horvath, M. (1974). The SCL-90 rating scale: First experience with the czech version in healthy male scientific workers. *Activitas Nervosa Superior*, 16, 115-116.
- Bouton, M. E., Mineka, S., & Barlow, D. H. (2001). A modern learning theory perspective on the etiology of panic disorder. *Psychological Review* 108, 4-32.
- Bowden, S. C., Fowler, K. S., Bell, R. C., Whelan, G., Clifford, C. C., Ritter, A. J., et al. (1998). The reliability and internal validity of the wisconsin card sorting test. [doi: 10.1080/713755573]. *Neuropsychological Rehabilitation*, 8(3), 243-254.
- Brand, M., Franke-Sievert, C., Jacoby, G. E., Markowitsch, H. J., & Tuschen-Caffier, B. (2007). Neuropsychological correlates of decision making in patients with bulimia nervosa. *Neuropsychology*, 21(6), 742-750.
- Bray, S., Barrowclough, C., & Lobban, F. (2007). The social problem-solving abilities of people with borderline personality disorder. *Behaviour Research and Therapy*, 45(6), 1409-1417.
- Bright, P., Jaldow, E., & Kopelman, M. D. (2002). The national adult reading test as a measure of premorbid intelligence: A comparison with estimates derived from demographic variables. *Journal of the International Neuropsychological Society*, 8(06), 847-854.
- Burgess, P. W. (2003). Assessment of executive function. In P. W. Halligan, U. Kischka & J. C. Marshall (Eds.), *Handbook of clinical neuropsychology*. Oxford; New York: Oxford University Press.
- Burgess, P. W., & Shallice, T. (1997). *The hayling and brixton tests*. Suffolk: Thames Valley Test Company.
- Button, E. J., Benson, E., Nollett, C., & Palmer, R. L. (2005). Don't forget EDNOS (eating disorder not otherwise specified): Patterns of service use in an eating disorders service. *Psychiatric Bulletin*, 29(4), 134-136.
- Carlat, D. J., & Camargo Jr, C. A. (1991). Review of bulimia nervosa in males. *American Journal of Psychiatry*, 148(7), 831-843.
- Castaneda, A. E., Suvisaari, J., Marttunen, M., Perala, J., Saarni, S. I., Aalto-Setälä, T., et al. (2011). Cognitive functioning in a population-based sample of young adults with anxiety disorders. 26(6), 346-353.
- Castaneda, A. E., Tuulio-Henriksson, A., Marttunen, M., Suvisaari, J., & Lonnqvist, J. (2008). A review on cognitive impairments in depressive and anxiety disorders with a focus on young adults. 106(1-2), 1-27.
- Castaneda, A. E., Tuulio-Henriksson, A., Marttunen, M., Suvisaari, J., & Lonnqvist, J. (2008). A review on cognitive impairments in depressive and anxiety disorders with a focus on young adults. [doi: 10.1016/j.jad.2007.06.006]. *Journal of Affective Disorders*, 106(1-2), 1-27.
- Castellini, G., Mannucci, E., Lo Sauro, C., Benni, L., Lazzeretti, L., Ravaldi, C., et al. (2012). Different moderators of cognitive-behavioral therapy on subjective

- and objective binge eating in bulimia nervosa and binge eating disorder: A three-year follow-up study. *Psychotherapy And Psychosomatics*, 81(1), 11-20.
- Castillo, E. P., Coy, P. E. C., Shejet, F. O., Duran, E. T., & Cabrera, D. M. (2010). Cognitive function evaluation: Attention and memory in panic disorder patients. *Salud Mental*, 33(6), 481-488.
- Cavedini, P., Riboldi, G., D'Annuncci, A., Belotti, P., Cisima, M., & Bellodi, L. (2002). Decision-making heterogeneity in obsessive-compulsive disorder: Ventromedial prefrontal cortex function predicts different treatment outcomes. *Neuropsychologia*, 40(2), 205-211.
- Cavedini, P., Zorzi, C., Bassi, T., Gorini, A., Baraldi, C., Ubbiali, A., et al. (2006). Decision-making functioning as a predictor of treatment outcome in anorexia nervosa. *Psychiatry Research*, 145, 179-187.
- Chang, E. C. (2002). Examining the link between perfectionism and psychological maladjustment: Social problem solving as a buffer. *Cognitive Therapy and Research*, 26(5), 581-595.
- Chang, E. C., & D'Zurilla, T. J. (1996). Relations between problem orientation and optimism, pessimism, and trait affectivity: A construct validation study. [doi: 10.1016/0005-7967(95)00046-1]. *Behaviour Research and Therapy*, 34(2), 185-194.
- Claes, L., Nederkoorn, C., Vandereycken, W., Guerrieri, R., & Vertommen, H. (2006). Impulsiveness and lack of inhibitory control in eating disorders. *Eating Behaviors*, 7(3), 196-203.
- Clark, D. M. (1986). A cognitive approach to panic. *Behaviour Research and Therapy*, 24, 461-470.
- Clark, D. M., Salkovskis, P. M., Oest, L.-G., Breitholz, E., Koehler, K. A., Westling, B. E., et al. (1997). Misinterpretation of body sensations in panic disorder. *Journal of Consulting and Clinical Psychology* 65, 203-213.
- Cooper, Z., Cooper, P. J., & Fairburn, C. G. (1989). The validity of the eating disorder examination and its subscales. *The British Journal of Psychiatry*, 154(6), 807-812.
- Cooper, Z., & Fairburn, C. G. (1987). The eating disorder examination: A semi-structured interview for the assessment of the specific psychopathology of eating disorders. *International Journal of Eating Disorders*(6), 1-8.
- Corral, M., Rodriguez, M., Amenedo, E., Sanchez, J. L., & Diaz, F. (2006). Cognitive reserve, age, and neuropsychological performance in healthy participants. *Developmental Neuropsychology*, 29(3), 479-491.
- Crawford, J. R., Deary, I. J., Starr, J. M., & Whalley, L. J. (2001). The NART as an index of prior intellectual functioning: A retrospective validity study covering a 66-year interval. *Psychological Medicine*, 31, 451-458.
- Crawford, J. R., Henry, J. D., Crombie, C., & Taylor, E. P. (2001). Brief report normative data for the hads from a large non-clinical sample. *British Journal of Clinical Psychology*, 40(4), 429.
- Crawford, J. R., Parker, D. M., Stewart, L. E., Besson, J. A. O., & De Lacey, G. (1989). Prediction of WAIS IQ with the National Adult Reading Test: Cross-validation and extension. *British journal of Clinical Psychology*, 28, 267-273.
- Crawford, J. R., Stewart, L. E., Garthwaite, P. H., Parker, D. M., & Besson, J. A. O. (1988). The relationship between demographic variables and NART

- performance in normal subjects. *British journal of Clinical Psychology*, 27, 181-182.
- CRD. (2008). *CRD's guidance for undertaking reviews in health care*: Centre for Reviews and Dissemination, University of York.
- Crombie, I. K., Brown, K. M. O., Irvine, L., Wrieden, W. L., Swanson, V., & Power, K. (2008). What maternal factors influence the diet of toddlers living in deprived areas: A cross-sectional survey? *Public Health Nutrition*(30), 1-7.
- D'Zurilla, T. J., & Maydeu-Olivares, A. (1995). Conceptual and methodological issues in social problem-solving assessment. *Behaviour Therapy*26(3), 409.
- D'Zurilla, T. J., Nezu, A. M., & Maydeu-Olivares, A. (1998). *Manual for the social problem solving inventory-revised*. North Tonawanda, New York: Multi-Health Systems.
- D'Zurilla, T. J., & Sheedy, C. F. (1992). The relation between social problem-solving ability and subsequent level of academic competence in college students. *Cognitive Therapy and Research*, 16(5), 589.
- D'Zurilla, T. J., & Maydeu-Oliveres, A. (1995). Conceptual and methodological issues in social problem-solving assessment. *Behaviour Therapy*(26), 409-432.
- D'Zurilla, T. J., Nezu, A. M., & Maydeu-Olivares, A. (2002). *Social problem-solving inventory-revised (SPSI-R)*. North Tonawanda, New York: Multi-Health Systems Inc.
- Deacon, B. J., & Abramowitz, J. S. (2005). The yale-brown obsessive compulsive scale: Factor analysis, construct validity, and suggestions for refinement. [doi: 10.1016/j.janxdis.2004.04.009]. *Journal of Anxiety Disorders*, 19(5), 573-585.
- Deckersbach, T., Moshier, S. J., Tuschen-Caffier, B., & Otto, M. W. (2011). Memory dysfunction in panic disorder: An investigation of the role of chronic benzodiazepine use. *Depression and Anxiety*, 28(11), 999-1007.
- Delis, D. C., Kaplan, E., & Kramer, J. H. (2001). *Delis-kaplin executive function system (dkefs): Technical manual*. San Antonio.Texas: : The Psychological Corporation.
- Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A. (1987). *California verbal learning test*. New York: The Psychological Corporation.
- Department of Health. (1998). *Data protection act*. Available from <http://www.legislation.gov.uk/ukpga/1998/29/contents>.
- Derogatis, L. R. (1983). *SCL-90-R administration, scoring & procedures manual-II*. Towson, MD: Clinical Psychometric Research.
- Derogatis, L. R. (1994). *SCL-90-R administration, scoring and procedures manual – third edition*. . Minneapolis: National Computer Systems Inc.
- Derogatis, L. R. (2000). SCL-90-R. In A. E. Kazdin (Ed.), *Encyclopedia of psychology*, vol. 7. (pp. 192-193): American Psychological Association, Oxford University Press.
- Derogatis, L. R., Lipman, R. S., & Covi, L. (1973). SCL-90, an outpatient psychiatric rating scale-preliminary report. *Psychopharmacology Bulletin*, 9, 13-28.
- Derogatis, L. R., Rickles, K., & Rock, A. F. (1976). SCL-90 and the MMPI: A step in the validation of a new self-report scale. *British Journal of Psychiatry*, 128, 280-289.

- Dudley, R., Kuyken, W., & Padesky, C. A. (2011). Disorder specific and trans-diagnostic case conceptualisation. *Clinical Psychology Review, 31*(2), 213-224.
- Egan, S. J., Wade, T. D., & Shafran, R. (2011). Perfectionism as a transdiagnostic process: A clinical review. [doi: 10.1016/j.cpr.2010.04.009]. *Clinical Psychology Review, 31*(2), 203-212.
- Ehlers, A., Margraf, J., Davies, S., & Roth, W. T. (1988). Selective processing of threat cues in subjects with panic attacks. *Cognition and Emotion, 2*, 201-219.
- Engel, S. G., Corneliussen, S. J., Wonderlich, S. A., Crosby, R. D., le Grange, D., Crow, S., et al. (2005). Impulsivity and compulsivity in bulimia nervosa. *The International Journal Of Eating Disorders, 38*(3), 244-251.
- Ennok, N. (2010). *The untested assumptions of schulte tables*. Paper presented at the The International Neuropsychological Society, The Polish Neuropsychological Society and The Polish Neuroscience Society Joint Mid-Year Meeting, Krakow. Poland.
- Fairburn, C. G., & Cooper, Z. (1993). The eating disorder examination (twelfth edition). In C. G. Fairburn & G. T. Wilson (Eds.), *Binge eating: Nature, assessment and treatment* (pp. 317-360). New York: Guilford Press.
- Fairburn, C. G., Cooper, Z., Bohn, K., O'Connor, M. E., Doll, H. A., & Palmer, R. L. (2007). The severity and status of Eating Disorder NOS: Implications for dsm-v. *Behaviour Research and Therapy, 45*(8), 1705-1715.
- Fairburn, C. G., Cooper, Z., & Shafran, R. (2003). Cognitive behaviour therapy for eating disorders: A "transdiagnostic" theory and treatment. *Behaviour Research and Therapy, 41*(5), 509-528.
- Federici, A., Summerfeldt, L. J., Harrington, J. L., McCabe, R. E., Purdon, C. L., Rowa, K., et al. (2010). Consistency between self-report and clinician-administered versions of the Yale-Brown Obsessive-Compulsive Scale. [doi: 10.1016/j.janxdis.2010.05.005]. *Journal of Anxiety Disorders, 24*(7), 729-733.
- Ferreri, F., Lapp, L. K., & Peretti, C. S. (2011). Current research on cognitive aspects of anxiety disorders. *Current Opinion in Psychiatry, 24*(1), 49-54.
- Fitch, M. I., Osoba, D., Iscoe, N., & Szalai, J. P. (1995). Predicting psychological distress in patients with cancer: Conceptual basis and reliability evaluation of a self-report questionnaire. *Anticancer Research, 15*(4), 1533-1542.
- Flashman, L. A., Horner, M. D., & Freides, D. (1991). Note on scoring perseveration on the wisconsin card sorting test. *The Clinical Neuropsychologist, 5*, 190-194.
- Fletcher, B., Gheorghe, A., Moore, D., Wilson, S., & Damery, S. (2012). Improving the recruitment activity of clinicians in randomised controlled trials: A systematic review. *BMJ open, 2*(1), e000496.
- Fletcher, J. M. (1985). Memory for verbal and nonverbal stimuli in learning disability subgroups: Analysis by selective reminding. *Journal of Experimental Child Psychology, 40*(2), 244-259.
- Franzen, M. D. (1989). *Reliability and validity in neuropsychological assessment*. New York: Plenum Press.
- Frost, R. O., Steketee, G., Krause, M. S., & Trepanier, K. L. (1995). The relationship of the Yale-Brown Obsessive Compulsive Scale (YBOCS) to other measures

- of obsessive compulsive symptoms in a nonclinical population. *Journal Of Personality Assessment*, 65(1), 158.
- Galderisi, S., Bucci, P., Mucci, A., Bellodi, L., Cassano, G. B., Santonastaso, P., et al. (2011). Neurocognitive functioning in bulimia nervosa: The role of neuroendocrine, personality and clinical aspects. *Psychological Medicine*, 41(4), 839-848.
- Galderisi, S., Mancuso, F., Mucci, A., Garramone, S., Zamboli, R., & Maj, M. (2008). Alexithymia and cognitive dysfunctions in patients with panic disorder. *Psychotherapy And Psychosomatics*, 77(3), 182-188.
- Garfinkel, P. E., Lin, E., Goering, P., Spegg, C., & et al. (1995). Bulimia nervosa in a canadian community sample: Prevalence and comparison of subgroups. *The American Journal Of Psychiatry*, 152(7), 1052.
- Gass, C. S., & Curiel, R. E. (2011). Test anxiety in relation to measures of cognitive and intellectual functioning. *Archives of Clinical Neuropsychology*, 26(5), 396-404.
- Giel, K. E., Wittorf, A., Wolkenstein, L., Klingberg, S., Drimmer, E., Schönenberg, M., et al. (In Press). Is impaired set-shifting a feature of “pure” anorexia nervosa? Investigating the role of depression in set-shifting ability in anorexia nervosa and unipolar depression. *Psychiatry Research*, <http://dx.doi.org.ezproxy.webfeat.lib.ed.ac.uk/10.1016/j.bbr.2011.03.031>.
- Gladsjo, J. A., Rapaport, M. H., McKinney, R., Lucas, J. A., Rabin, A., Oliver, T., et al. (1998). A neuropsychological study of panic disorder: Negative findings. *Journal of Affective Disorders*, 49(2), 123-131.
- Gohier, B., Ferracci, L., Surguladze, S. A., Lawrence, E., El Hage, W., Kefi, M. Z., et al. (2009). Cognitive inhibition and working memory in unipolar depression. [doi: 10.1016/j.jad.2008.10.028]. *Journal of Affective Disorders*, 116(1-2), 100-105.
- Goldner, E. M., Geller, J., Birmingham, C. L., & Remick, R. A. (2000). Comparison of shoplifting behaviours in patients with eating disorders, psychiatric control subjects, and undergraduate control subjects. *Canadian Journal Of Psychiatry. Revue Canadienne De Psychiatrie*, 45(5), 471-475.
- Goodman, W. K., Price, L. H., Rasmussen, S. A., & Mazure, C. (1989). The Yale-Brown Obsessive Compulsive Scale: Ii. Validity. *Archives of General Psychiatry*, 46(11), 1012-1016.
- Goodman, W. K., Price, L. H., Rasmussen, S. A., Mazure, C., Fleischmann, R. L., Hill, C. L., et al. (1989). The Yale Brown Obsessive Compulsive Scale. I. Development, use and reliability. *Archives of General Psychiatry*, 46, 1006-1011.
- Gordeev, S. A. (2008). Cognitive functions and the state of nonspecific brain systems in panic disorders. *Neuroscience & Behavioral Physiology*, 38(7), 707-714.
- Gordon, K. H., Denoma, J. M., Bardone, A. M., Abramson, L. Y., & Joiner, T. E. J. (2005). Original research: Self-competence and the prediction of bulimic symptoms in older women. *Behavior Therapy*, 36, 169-175.
- Gorini, A., Schruers, K., Riva, G., & Griez, E. (2010). Nonhomogeneous results in place learning among panic disorder patients with agoraphobia. [doi: 10.1016/j.psychres.2009.10.002]. *Psychiatry Research*, 179(3), 297-305.
- Graver, C. J., & White, P. M. (2007). Neuropsychological effects of stress on social phobia with and without comorbid depression. [doi:

- 10.1016/j.brat.2006.08.002]. *Behaviour Research and Therapy*, 45(6), 1193-1206.
- Guillaume, S., Sang, C. N. T., Jaussent, I., Raingeard, I., Bringer, J., Jollant, F., et al. (2010). Is decision making really impaired in eating disorders? *Neuropsychology*, 24(6), 808-812.
- Haaga, D. A. F., Fine, J. A., Terrill, D. R., Stewart, B. L., & Beck, A. T. (1995). Social problem-solving deficits, dependency, and depressive symptoms. *Cognitive Therapy and Research*, 19(2), 147-158.
- Hagenaars, M. A., van Minnen, A., Hoogduin, C. A. L., & Verbraak, M. (2009). A transdiagnostic comparison of trauma and panic memories in ptsd, panic disorder, and healthy controls. *Journal of Behavior Therapy and Experimental Psychiatry*, 40(3), 412-422.
- Hanten, G., Cook, L., Orsten, K., Chapman, S. B., Li, X., Wilde, E. A., et al. (2011). Effects of traumatic brain injury on a virtual reality social problem solving task and relations to cortical thickness in adolescence. *Neuropsychologia*, 49(3), 486-497.
- Haugh, J. A. (2006). Specificity and social problem-solving: Relation to depressive and anxious symptomology. *Journal of Social and Clinical Psychology*, 25(4), 392-403.
- Heaton, R. K., Chelune, G. J., Talley, J. L., Kay, G. G., & Curtiss, G. (1993). *Wisconsin Card Sorting Test Manual: Revised and expanded*. Florida: Psychological Assessment Resources Inc.
- Herpertz-Dahlmann, B., & Remschmidt, H. (1993). Depression and psychosocial adjustment in adolescent anorexia nervosa. A controlled 3-year follow-up study. *European Child & Adolescent Psychiatry*, 2(3), 146-154.
- Herrera-Guzman, I., Gudayol-Ferre, E., Jarne-Esparcia, A., Herrera-Abarca, J. E., Herrera-Guzman, D., Pero-Cebollero, M., et al. (2009). Comorbidity of anxiety disorders in major depressive disorder. A clinical trial to evaluate neuropsychological deficit. *The European Journal of Psychiatry*, 23(1), 5-18.
- Higgins, J., & Altman, D. (2008). Chapter 8: Assessing risk of bias in included studies. In J. Higgins & S. Green (Eds.), *Cochrane handbook for systematic reviews of interventions version 5.0.1 (updated september 2008)*. The Cochrane Collaboration, 2008. Available from www.cochrane-handbook.org.
- Holi, M. M. (2003). *Assessment of psychiatric symptoms using the SCL-90*. Helsinki University, Helsinki.
- Holi, M. M., Marttunen, M., & Aalberg, V. (2003). Comparison of the GHQ-36, the GHQ-12 and the SCL-90 as psychiatric screening instruments in the finnish population. *Nordic Journal of Psychiatry*, 57(3), 233-238.
- Horowitz, L. M., Rosenberg, S. E., Baer, B. A., Ureno, G., & Villasensor, V. S. (1988). Inventory of interpersonal problems: Psychometric properties and clinical applications. *Journal of Consulting and Clinical Psychology*, 56(6), 885-892.
- Hudson, J. I., Hiripi, E., Pope, H. G., & Kessler, R. C. (2007). The prevalence and correlates of eating disorders in the national comorbidity survey replication. *Biological psychiatry*, 61(3), 348-358.
- Ingram, F., Greve, K. W., Ingram, P. T. F., & Soukup, V. M. (1999). Temporal stability of the wisconsin card sorting test in an untreated patient sample. *British Journal of Clinical Psychology*, 38(2), 209-211.

- Jacobs, W. J., Laurance, H. E., & Thomas, K. G. F. (1997). Place learning in virtual space i: Acquisition, overshadowing, and transfer. [doi: 10.1006/lmot.1997.0977]. *Learning and Motivation*, 28(4), 521-541.
- Kaplan, J. S., Erickson, K., Luckenbaugh, D. A., Weiland-Fiedler, P., Geraci, M., Sahakian, B. J., et al. (2006). Differential performance on tasks of affective processing and decision-making in patients with panic disorder and panic disorder with comorbid major depressive disorder. [doi: 10.1016/j.jad.2006.04.016]. *Journal of Affective Disorders*, 95(1-3), 165-171.
- Kaye, L. H. (2005). Comorbidity of anxiety disorders with anorexia and bulimia nervosa. *The American Journal Of Psychiatry*, 161(12), 2215-2221.
- Keefe, R. S. (1995). The contribution of neuropsychology to psychiatry. *The American Journal Of Psychiatry*, 152(1), 6-15.
- Kemps, E., & Wilsdon, A. (2010). Preliminary evidence for a role for impulsivity in cognitive disinhibition in bulimia nervosa. *Journal Of Clinical And Experimental Neuropsychology*, 32(5), 515-521.
- Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of dsm-iv disorders in the national comorbidity survey replication. *Archives of General Psychiatry*, 62(6), 593-602.
- Kessler, R. C., Chiu, W. T., Jin, R., Ruscio, A. M., Shear, K., & Walters, E. E. (2006). The epidemiology of panic attacks, panic disorder, and agoraphobia in the national comorbidity survey replication. *Archives of General Psychiatry*, 63(4), 415-424.
- Kiezebrink, K., Crombie, I. K., Irvine, L., Swanson, V., Power, K., & Wrieden, W. L. (2009). Strategies for achieving a high response rate in a home interview survey. *BMC Medical research and Methodology*, 30, 46.
- Kim, S. W., Dysken, M. W., & Kuskowski, M. (1990). The yale-brown-obsessive-compulsive-scale: A reliability and validity study. *Psychiatry Research*, 34, 99-106.
- Kim, S. W., Dysken, M. W., & Kuskowski, M. (1992). The symptom check list 90: A reliability and validity study. *Psychiatry Research*, 41, 37-44.
- Kingston, K., Szmukler, G., Andrewes, D., Tress, B., & Desmond, P. (1996). Neuropsychological and structural brain changes in anorexia nervosa before and after refeeding. *Psychological Medicine*, 26(1), 15-28.
- Kirisci, L., Tarter, R. E., Vanyukov, M., Reynolds, M., & Habeych, M. (2004). Relation between cognitive distortions and neurobehavior disinhibition on the development of substance use during adolescence and substance use disorder by young adulthood: A prospective study. [doi: 10.1016/j.drugalcdep.2004.04.015]. *Drug and Alcohol Dependence*, 76(2), 125-133.
- Klein, D. N., Leon, A. C., Li, C., D'Zurilla, T. J., Black, S. R., Vivian, D., et al. (2011). Social problem solving and depressive symptoms over time: A randomized clinical trial of cognitive-behavioral analysis system of psychotherapy, brief supportive psychotherapy, and pharmacotherapy. *Journal of Consulting and Clinical Psychology*, 79(3), 342-352.
- Koeter, M. W. J. (1992). Validity of the GHQ and SCL anxiety and depression scales: A comparative study. [doi: 10.1016/0165-0327(92)90112-J]. *Journal of Affective Disorders*, 24(4), 271-279.

- Konstantakopoulos, G., Tchanturia, K., Surguladze, S. A., & David, A. S. (2011). Insight in eating disorders: Clinical and cognitive correlates. *Psychological Medicine*, 41(09), 1951-1961.
- Krug, I., Casanovas, C., Granero, R., Martinez, C., Jimenez-Murcia, S., Bulik, C., et al. (2008). Comparison study of full and subthreshold bulimia nervosa: Personality, clinical characteristics, and short-term response to therapy. *Psychotherapy Research*, 18(1), 37-47.
- Kuelz, A. K., Hohagen, F., & Voderholzer, U. (2004). Neuropsychological performance in obsessive-compulsive disorder: A critical review. [doi: 10.1016/j.biopsycho.2003.07.007]. *Biological Psychology*, 65(3), 185-236.
- Kurtz, M., Moberg, P., Gur, R., & Gur, R. (2001). Approaches to cognitive remediation of neuropsychological deficits in schizophrenia: A review and meta-analysis. *Neuropsychology Review*, 11(4), 197-210.
- Langenecker, S. A., Zubieta, J. K., Young, E. A., Akil, H., & Nielson, K. A. (2007). A task to manipulate attentional load, set-shifting, and inhibitory control: Convergent validity and test-retest reliability of the Parametric Go/No-Go test. *Journal Of Clinical And Experimental Neuropsychology*, 29(8), 842-853.
- Lauer, C. J., Gorzewski, B., Gerlinghoff, M., Backmund, H., & Zihl, J. (1999). Neuropsychological assessments before and after treatment in patients with anorexia nervosa and bulimia nervosa. *Journal of Psychiatric Research*, 33(2), 129-138.
- Lautenbacher, S., Sernal, J., & Krieg, J. C. (2002). Divided and selective attention in panic disorder. A comparative study of patients with panic disorder, major depression and healthy controls. *European Archives of Psychiatry & Clinical Neuroscience*, 252(5), 210-213.
- Lezak, M. D., Howieson, D. B., & Loring, D. W. (2004). *Neuropsychological assessment 4th edition*. New York: Oxford University Press.
- Londahl, E. A., Tverskoy, A., & D'Zurilla, T. J. (2005). The relations of internalizing symptoms to conflict and interpersonal problem solving in close relationships. *Cognitive Therapy and Research*, 29(4), 445-462.
- Lopez, C. A., Tchanturia, K., Stahl, D., & Treasure, J. (2008). Central coherence in women with bulimia nervosa. *International Journal of Eating Disorders*, 41(4), 340-347.
- Lowe, P. A., Mayfield, J. W., & Reynolds, C. R. (2003). Gender differences in memory test performance among children and adolescents. *Archives of Clinical Neuropsychology*, 18(8), 865-878.
- Lucas, J. A., Telch, M. J., & Bigler, E. D. (1991). Memory functioning in panic disorder: A neuropsychological perspective. [doi: 10.1016/0887-6185(91)90013-J]. *Journal of Anxiety Disorders*, 5(1), 1-20.
- Ludewig, S., Paulus, M. P., Ludewig, K., & Vollenweider, F. X. (2003). Decision-making strategies by panic disorder subjects are more sensitive to errors. [doi: 10.1016/S0165-0327(02)00089-7]. *Journal of Affective Disorders*, 76(1-3), 183-189.
- Lundh, L. G., Wikstrom, J., Westerlund, J., & Ost, L. G. (1999). Preattentive bias for emotional information in panic disorder with agoraphobia. *Journal of Abnormal Psychology*, 108, 222-232.

- Lyche, P., Jonassen, R., Stiles, T. C., Ulleberg, P., & Landro, N. I. (2011). Verbal memory functions in unipolar major depression with and without co-morbid anxiety. *The Clinical Neuropsychologist*, 25(3), 359-375.
- Mar, R. A., DeYoung, C. G., Higgins, D. M., & Peterson, a. B. (2006). Self-liking and self-competence separate self-evaluation from self-deception: Associations with personality, ability, and achievement. *Journal of Personality*, 74(4), 1047-1078.
- Martin, C. K., Williamson, D. A., & Thaw, J. M. (2000). Criterion validity of the multi-axial assessment of eating disorders symptoms. *International Journal of Eating Disorders*, 28(3), 303-310.
- Martinez-Gonzalez, A. E., & Piqueras-Rodriguez, J. A. (2008). Neuropsychological update on obsessive-compulsive disorder. *Revista De Neurologia*, 46(10), 618-625.
- Mataix-Cols, D., Alonso, P., Pifarré, J., Menchón, J. M., & Vallejo, J. (2002). Neuropsychological performance in medicated vs. Unmedicated patients with obsessive-compulsive disorder. *Psychiatry Research*, 109(3), 255-264.
- Mataix-Cols, D., & van den Heuvel, O. A. (2006). Common and distinct neural correlates of obsessive-compulsive and related disorders. *Psychiatric Clinics of North America*, 29(2), 391-410.
- Matsunaga, H., Kiriike, N., Miyata, A., Iwasaki, Y., Matsui, T., Fujimoto, K., et al. (1999). Prevalence and symptomatology of comorbid obsessive-compulsive disorder among bulimic patients. *Psychiatry And Clinical Neurosciences*, 53(6), 661-666.
- McClintock, S. M., Husain, M. M., Greer, T. L., & Cullum, C. M. (2010). Association between depression severity and neurocognitive function in major depressive disorder: A review and synthesis. *Neuropsychology*, 24(1), 9-34.
- McFillin, R. K. (2009). The social problem-solving approach of adolescent females diagnosed with an eating disorder :Toward a greater understanding of control. *Psychology Dissertations, Paper 102*, http://digitalcommons.pcom.edu/psychology_dissertations/102.
- McMurran, M., Blair, M., & Egan, V. (2002). An investigation of the correlations between aggression, impulsiveness, social problem-solving, and alcohol use. *Aggressive Behavior*, 28(6), 439-445.
- Mehler, P. S., Sabel, A. L., Watson, T., & Andersen, A. E. (2008). High risk of osteoporosis in male patients with eating disorders. *The International Journal Of Eating Disorders*, 41(7), 666-672.
- Menzies, L., Chamberlain, S. R., Laird, A. R., Thelen, S. M., Sahakian, B. J., & Bullmore, E. T. (2008). Integrating evidence from neuroimaging and neuropsychological studies of obsessive-compulsive disorder: The orbitofronto-striatal model revisited. [doi: 10.1016/j.neubiorev.2007.09.005]. *Neuroscience and Biobehavioral Reviews*, 32(3), 525-549.
- Merriam, E. P., Thase, M. E., Haas, G. L., Keshavan, M. S., & Sweeney, J. A. (1999). Prefrontal cortical dysfunction in depression determined by Wisconsin Card Sorting Test Performance. *The American Journal Of Psychiatry*, 156(5), 780-782.
- Miles, J., & Shevlin, M. (2001). *Applying regression and correlation: A guide for students and researchers*. London: Sage Publications.

- Millan, M. J., Agid, Y., Brüne, M., Bullmore, E. T., Carter, C. S., Clayton, N. S., et al. (2012). Cognitive dysfunction in psychiatric disorders: Characteristics, causes and the quest for improved therapy. [10.1038/nrd3628]. *Nat Rev Drug Discov*, 11(2), 141-168.
- Moritz, M., Beat, M., Klos, M., Jacobsen, D., Wein, C., Fricke, S., et al. (2002). Dimensional structure of the yale brown obsessive-compulsive scale (YBOCS). *Psychiatry Research*, 109, 193-199.
- Murphy, R., Nutzinger, D. O., Paul, T., & Leplow, B. (2004). Conditional-associative learning in eating disorders: A comparison with OCD. *Journal Of Clinical And Experimental Neuropsychology*, 26(2), 190-199.
- Naylor, H., Mountford, V., & Brown, G. (2011). Beliefs about excessive exercise in eating disorders: The role of obsessions and compulsions. *European Eating Disorders Review*, 19(3), 226-236.
- Nelson, H. E. (1982). *National Adult Reading Test (NART): Test manual*. London: NFER Nelson Publishing Co Ltd.
- Nelson, H. E., & Willison, J. (1991). *National Adult Reading Test (NART). Test manual, 2nd*. London, UK: NFER-Nelson.
- NHS QIS. (2006). *Eating disorders in scotland: Recommendations for management and treatment*. Available from www.nhshealthquality.org.
- NHS Tayside Information Governance. (2010). *NHS tayside information governance policy. Version 2.1*.
- NICE. (2004a). *Eating disorders: Core interventions in the treatment and management of anorexia nervosa, bulimia nervosa and related eating disorders. Clinical Guideline 9*. London: National Institute for Health and Clinical Excellence. Available from www.nice.org.uk.
- NICE. (2004b). *Self-harm: The physical and psychological management and secondary prevention of self-harm in primary and secondary care. Clinical guideline 16*. London: National Institute for Health and Clinical Excellence.
- NICE. (2010). *Depression: The treatment and management of depression in adults (updated edition) CG90*. London: National Institute for Health and Clinical Excellence.
- NICE. (2011). *Generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults. NICE clinical guideline 113*. London: National Institute for Health and Clinical Excellence.
- O'Toole, M. S., & Pedersen, A. D. (2011). A systematic review of neuropsychological performance in social anxiety disorder. *Nordic Journal of Psychiatry*, 65(3), 147-161.
- Olley, A., Malhi, G., & Sachdev, P. (2007). Memory and executive functioning in obsessive-compulsive disorder: A selective review. [doi: 10.1016/j.jad.2007.02.023]. *Journal of Affective Disorders*, 104(1-3), 15-23.
- Patel, M. X., Doku, V., & Tennakoon, L. (2003). Challenges in recruitment of research participants. *Advances in Psychiatric Treatment*, 9(3), 229-238.
- Paterson, G., Power, K., Collin, P., Greirson, D., Yellowlees, A., & Park, K. (2011). A mediational model of self-esteem and social problem-solving in anorexia nervosa. *European Eating Disorders Review*, 19(2), 112-120.
- Paterson, G., Power, K., Yellowlees, A., Park, K., & Taylor, L. (2007). The relationship between two-dimensional self-esteem and problem solving style

- in an anorexic inpatient sample. *European Eating Disorders Review*, 15(1), 70-77.
- Paulus, M. P. (1997). Long-range interactions in sequences of human behavior. *Physical Review E*, 55(3249-3256).
- Peveler, R. C., & Fairburn, C. G. (1990). Measurement of neurotic symptoms by self-report questionnaire: Validity of the SCL-90-R. *Psychological Medicine*, 20(04), 873-879.
- Phan, K. L., Orlichenko, A., Boyd, E., Angstadt, M., Coccaro, E. F., Liberzon, I., et al. (2009). Preliminary evidence of white matter abnormality in the uncinate fasciculus in generalized social anxiety disorder. *Biological psychiatry*, 66(7), 691-694.
- Polak, A. R., Witteveen, A. B., Reitsma, J. B., & Olff, M. (2012). The role of executive function in posttraumatic stress disorder: A systematic review. [doi: 10.1016/j.jad.2012.01.001]. *Journal of Affective Disorders*, in press/available online February 2012(0).
- Porter, R. J., Bourke, C., & Gallagher, P. (2007). Neuropsychological impairment in major depression: Its nature, origin and clinical significance. *The Australian And New Zealand Journal Of Psychiatry*, 41(2), 115-128.
- Purcell, R., Maruff, P., Kyrios, M., & Pantelis, C. (1998). Neuropsychological deficits in obsessive-compulsive disorder: A comparison with unipolar depression, panic disorder, and normal controls. *Archives of General Psychiatry*, 55(5), 415-423.
- Rauter, U. K., Leonard, C. E., & Swett, C. P. (1996). SCL-90-R factor structure in an acute, involuntary, adult psychiatric inpatient sample. [Article]. *Journal of Clinical Psychology*, 52(6), 625-629.
- Reiman, E. M., Fusselman, M. J., Fox, P. T., & Raichle, M. E. (1989). Neuroanatomical correlates of anticipatory anxiety. *Science*, 243(4894), 1071-1074.
- Reiman, E. M., Raichle, M. E., Robins, E., Mintun, M. A., Fusselman, M. J., Fox, P. T., et al. (1989). Neuroanatomical correlates of a lactate-induced anxiety attack. *Archives Of General Psychiatry*, 46(6), 493-500.
- Reitan, R. M., & Davidson, L. A. (1974). *Clinical neuropsychology: Current status and applications*. New York: Wiley.
- Reitan, R. M., & Wolfson, D. (1995). Influence of age and education on neuropsychological test results. *The Clinical Neuropsychologist*, 9(2), 151-158.
- Rey, A. (1941). L'examen psychologique dans les cas d'encephalopathie traumatique.(les problems.). *Archives de Psychologie*, 28, 215-285.
- Ricca, V., Mannucci, E., Mezzani, B., Di Bernardo, M., Zucchi, T., Paionni, A., et al. (2001). Psychopathological and clinical features of outpatients with an eating disorder not otherwise specified. *Eating and Weight Disorders*, 6(3), 157-165.
- Robbins, T. W., Gillan, C. M., Smith, D. G., de Wit, S., & Ersche, K. D. (2012). Neurocognitive endophenotypes of impulsivity and compulsivity: Towards dimensional psychiatry. [doi: 10.1016/j.tics.2011.11.009]. *Trends in Cognitive Sciences*, 16(1), 81-91.

- Roberts, M. E., Tchanturia, K., Stahl, D., Southgate, L., & Treasure, J. (2007). A systematic review and meta-analysis of set-shifting ability in eating disorders. *Psychological Medicine*, 37(8), 1075-1084.
- Roberts, M. E., Tchanturia, K., & Treasure, J. L. (2010). Exploring the neurocognitive signature of poor set-shifting in anorexia and bulimia nervosa. *Journal of Psychiatric Research*, 44(14), 964-970.
- Robinson, M. D., Pearce, E. A., Engel, S. G., & Wonderlich, S. A. (2009). Cognitive control moderates relations between impulsivity and bulimic symptoms. *Cognitive Therapy and Research*, 33(4), 356-367.
- Rockert, W., Kaplan, A. S., & Olmsted, M. P. (2007). Eating disorder not otherwise specified: The view from a tertiary care treatment center. *The International Journal Of Eating Disorders*, 40 Suppl, S99-S103.
- Rogers, R., Everitt, B., Baldacchino, A., Blackshaw, A., Swainson, R., Wynne, K., et al. (1999). Dissociable deficits in the decision-making cognition of chronic amphetamine abusers, opiate abusers, patients with focal damage to prefrontal cortex, and tryptophan-depleted normal volunteers: Evidence for monoaminergic mechanisms. *Neuropsychopharmacology*, 20(4), 322-339.
- Rosen, J. C., Vara, L., Wendt, S., & Leitenberg, H. (1990). Validity studies of the eating disorder examination. *International Journal of Eating Disorders*, 9(5), 519-528.
- Rosenberg, M. (1962). The association between self-esteem and anxiety. *Journal of Psychiatric Research*, 1(2), 135-152.
- Rosenberg, M. (1965). *Society and the adolescent self-image*. Princeton, NJ: Princeton University Press.
- Rosval, L., Steiger, H., Bruce, K., Israël, M., Richardson, J., & Aubut, M. (2006). Impulsivity in women with eating disorders: Problem of response inhibition, planning, or attention? *The International Journal Of Eating Disorders*, 39(7), 590-593.
- Ruuska, J., Kaltiala-Heino, R., Rantanen, P., & Koivisto, A.-M. (2005). Psychopathological distress predicts suicidal ideation and self-harm in adolescent eating disorder outpatients. *European Child & Adolescent Psychiatry*, 14(5), 276-281.
- Schmidt, U., Landau, S., Pombo-Carril, M. G., Bara-Carril, N., Reid, Y., Murray, K., et al. (2006). Does personalized feedback improve the outcome of cognitive-behavioural guided self-care in bulimia nervosa? A preliminary randomized controlled trial. *British Journal of Clinical Psychology*, 45(1), 111-121.
- Scottish Executive. (2003). NHS code of practice on protecting patient confidentiality.
- Silverstone, P. H., & Salsali, M. (2003). Low self-esteem and psychiatric patients: Part i – the relationship between low self-esteem and psychiatric diagnosis. *Annals of General Hospital Psychiatry*, 2(2).
- Southgate, L., Tchanturia, K., & Treasure, J. (2008). Information processing bias in anorexia nervosa. *Psychiatry Research*, 160(2), 221-227.
- Spernal, J., Krieg, J. C., & Lautenbacher, S. (2003). Pain thresholds as a putative functional test for cerebral laterality in major depressive disorder and panic disorder. *Neuropsychobiology*, 48(3), 146-151.

- Stein, R. A., & Strickland, T. L. (1998). A review of the neuropsychological effects of commonly used prescription medications. *Archives of Clinical Neuropsychology*, 13(3), 259-284.
- Steketee, G., Frost, R., & Bogart, K. (1995). The Yale-Brown Obsessive Compulsive Scale: Interview versus self report. *Behaviour Research and Therapy*, 34(8), 675-684.
- Stordal, K. I., Lundervold, A. J., Egeland, J., Mykletun, A., Asbjørnsen, A., Landrø, N. I., et al. (2004). Impairment across executive functions in recurrent major depression. *Nordic Journal of Psychiatry*, 58(1), 41-47.
- Surgenor, L. J., Maguire, S., Russell, J., & Touyz, S. (2007). Self-liking and self-competence: Relationship to symptoms of anorexia nervosa. *European Eating Disorders Review*, 15(2), 139-145.
- Svaldi, J., Dorn, C., & Trentowska, M. (2011). Effectiveness for interpersonal problem-solving is reduced in women with binge eating disorder. *European Eating Disorders Review*, 19(4), 331-341.
- Swanson, H., Power, K., Collin, P., Deas, S., Paterson, G., Grierson, D., et al. (2010). The relationship between parental bonding, social problem solving and eating pathology in an anorexic inpatient sample. *European Eating Disorders Review*, 18(1), 22-32.
- Szeszko, P. R., Ardekani, B. A., Ashtari, M., Malhotra, A. K., Robinson, D. G., Bilder, R. M., et al. (2005). White matter abnormalities in obsessive-compulsive disorder: A diffusion tensor imaging study. *Archives of General Psychiatry*, 62(7), 782-790.
- Tabachnick, B. G., & Fidell, L. S. (2001). *Using multivariate analysis* (Vol. 4th edition). Boston: Allyn and Bacon.
- Tabarés-Seisdedos, R., Balanzá-Martínez, V., Sánchez-Moreno, J., Martínez-Aran, A., Salazar-Fraile, J., Selva-Vera, G., et al. (2008). Research report: Neurocognitive and clinical predictors of functional outcome in patients with schizophrenia and bipolar i disorder at one-year follow-up. *Journal of Affective Disorders*, 109, 286-299.
- Tafarodi, R. W., & Milne, A. B. (2002). Decomposing global self-esteem. *Journal of Personality*, 70(4), 443-484.
- Tafarodi, R. W., & Swann, W. B. (2001). Two dimensional self-esteem: Theory and measurement. *Personality and Individual Differences*(31), 653-673.
- Takagishi, Y., Sakata, M., & Kitamura, T. (2011). Effects of self-esteem on state and trait components of interpersonal dependency and depression in the workplace. [Article]. *Journal of Clinical Psychology*, 67(9), 918-926.
- Tayside Medical Science Centre. (2011). *Standard operating procedure for electronic archiving of clinical trial data*.
- Tchanturia, K., Anderluh, M. B., Morris, R. G., Rabe-Hesketh, S., Collier, D. A., Sanchez, P., et al. (2004). Cognitive flexibility in anorexia nervosa and bulimia nervosa. *Journal of the International Neuropsychological Society*, 10(4), 513-520.
- Tchanturia, K., Davies, H., Lopez, C., Schmidt, U., Treasure, J., & Wykes, T. (2008). Neuropsychological task performance before and after cognitive remediation in anorexia nervosa: A pilot case-series. *Psychological Medicine*, 38(9), 1371-1373.

- Tchanturia, K., Davies, H., & Campbell, I. C. (2007). Cognitive remediation therapy for patients with anorexia nervosa: Preliminary findings. *Annals of General Psychiatry*, 6(14).
- Tchanturia, K., Morris, R. G., Anderluh, M. B., Collier, D. A., Nikolaou, V., & Treasure, J. (2004). Set shifting in anorexia nervosa: An examination before and after weight gain, in full recovery and relationship to childhood and adult ocpd traits. *Journal of Psychiatric Research*, 38(5), 545-552.
- Teachman, B. A., Smith-Janik, S. B., & Saporito, J. (2007). Information processing biases and panic disorder: Relationships among cognitive and symptom measures. *Behaviour Research and Therapy*, 45, 1791-1811.
- Tobin, D. L., Griffing, A., & Griffing, S. (1997). An examination of subtype criteria for bulimia nervosa. *The International Journal Of Eating Disorders*, 22(2), 179-186.
- Trahan, D. E., & Larrabee, G. J. (1989). *Continuous visual memory test*. Odessa, FL: Psychological Assessment Resources.
- Treasure, J., Claudino, A., M., & Zucker, N. (2010). Eating disorders. *The Lancet*, 375(9714), 583-593.
- Treweek, S., Mitchell, E., Pitkethly, M., Cook, J., Kjeldstrøm, M., Taskila, T., et al. (2010). Strategies to improve recruitment to randomised controlled trials. *Cochrane Database of Systematic Reviews* (1), Art. No.: MR000013.
- Trivedi, J. K. (2006). Cognitive deficits in psychiatric disorders: Current status. *Indian Journal Of Psychiatry*, 48(1), 10-20.
- Van den Eynde, F., Guillaume, S., Broadbent, H., Stahl, D., Campbell, I. C., Schmidt, U., et al. (2011). Neurocognition in bulimic eating disorders: A systematic review. *Acta Psychiatrica Scandinavica*, 124(2), 120-140.
- Van den Eynde, F., Samarawickrema, N., Kenyon, M., DeJong, H., Lavender, A., Startup, H., et al. (2012). A study of neurocognition in bulimia nervosa and eating disorder not otherwise specified-bulimia type. *Journal Of Clinical And Experimental Neuropsychology*, 34(1), 67-77.
- van den Heuvel, O. A., Veltman, D. J., Groenewegen, H. J., Witter, M. P., Merkelbach, I., Cath, D. C., et al. (2005). Disorder-specific neuroanatomical correlates of attentional bias in obsessive-compulsive disorder, panic disorder, and hypochondriasis. *Archives of General Psychiatry*, 62(8), 922-933.
- Vandenberg, S. G., & Kuse, A. R. (1978). Mental rotations, a group test of three-dimensional spatial visualization. *Perceptual and Motor Skills*, 47, 599-604.
- Vandromme, H., Hermans, D., Spruyt, A., & Eelen, P. (2007). Dutch translation of the self-liking/self-competence scale – revised: A confirmatory factor analysis of the two-factor structure. *Personality and Individual Differences*, 42, 157-167.
- Verdejo-García, A., Bechara, A., Recknor, E. C., & Pérez-García, M. (2006). Executive dysfunction in substance dependent individuals during drug use and abstinence: An examination of the behavioral, cognitive and emotional correlates of addiction. *Journal of the International Neuropsychological Society*, 12(03), 405-415.
- Vlaar, A. M. M., & Wade, D. T. (2003). Verbal fluency assessment of patients with multiple sclerosis: Test–retest and inter-observer reliability. *Clinical Rehabilitation*, 17(7), 756.

- Vythilingam, M., Anderson, E. R., Goddard, A., Woods, S. W., Staib, L. H., Charney, D. S., et al. (2000). Temporal lobe volume in panic disorder - a quantitative magnetic resonance imaging study. *Psychiatry Research-Neuroimaging*, 99(2), 75-82.
- Warrington, E. K. (1984). *Recognition memory test*. Windsor, UK: NFER-Nelson.
- Watson, J. M., & Torgerson, D. J. (2006). Increasing recruitment to randomised trials: A review of randomised controlled trials. *BMC medical research methodology*, 6, 34.
- Waxman, S. E. (2009). A systematic review of impulsivity in eating disorders. *European Eating Disorders Review*, 17(6), 408-425.
- Wechsler, D. (1981). *Wechsler adult intelligence scale-revised (WAIS-R)*: The Psychological Corporation.
- Wechsler, D. (1987). *Wechsler memory scale-revised manual*. San Antonio, TX: The Psychological Corporation.
- WHO. (2010). *International classification of diseases, 10th revision, 2nd edition*. Geneva: World Health Organisation.
- Wilson, G. T., & Smith, D. (1989). Assessment of bulimia nervosa: An evaluation of the eating disorders examination. *International Journal of Eating Disorders*, 8(2), 173-179.
- Woody, S. R., Steketee, G., & Chambless, D. L. (1995). Reliability and validity of the yale-brown obsessive compulsive scale. *Behaviour Research and Therapy*, 33, 597-605.
- Xu, G., Lin, K., Rao, D., Dang, Y., Ouyang, H., Guo, Y., et al. (2012). Neuropsychological performance in bipolar I, bipolar II and unipolar depression patients: A longitudinal, naturalistic study. *Journal of Affective Disorders*, 136(3), 328-339.
- Zack, M., Toneatto, T., & Streiner, D. L. (1998). The SCL-90 factor structure in comorbid substance abusers. *10*(1), 85-101.
- Zakzanis, K. K., Campbell, Z., & Polsinelli, A. (2010). Quantitative evidence for distinct cognitive impairment in anorexia nervosa and bulimia nervosa. *Journal Of Neuropsychology*, 4(Pt 1), 89-106.
- Zaslavsky, A., Zaborski, L., & Cleary, P. (2002). Factors affecting response rates to the consumer assessment of health plans study survey. *Medical Care*, 40(6), 485-499.
- Zeeck, A., Birindelli, E., Sandholz, A., Joos, A., Herzog, T., & Hartmann, A. (2007). Symptom severity and treatment course of bulimic patients with and without a borderline personality disorder. *European Eating Disorders Review: The Journal Of The Eating Disorders Association*, 15(6), 430-438.
- Zigmond, A., & Snaith, R. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica*, 67, 361-370.

Appendices

Appendix 1 Author Guidelines for Journal of Affective Disorders

Journal of Affective Disorders

Guide for Authors

Submission of a manuscript implies that it contains original work and has not been published or submitted for publication elsewhere. It also implies the transfer of the copyright from the author to the publisher. Authors should include permission to reproduce any previously published material. Any potential conflict of interest should be disclosed in the cover letter. Authors are also requested to include contact information (name, address, telephone, fax, and e-mail) for three potential peer reviewers, to be used at the Editor's discretion. The review process requires 2 to 5 months.

Ethics in publishing

For information on Ethics in publishing and Ethical guidelines for journal publication (including the necessity to avoid plagiarism and duplicate publication) see <http://www.elsevier.com/ethicalguidelines> and <http://www.elsevier.com/publishingethics>

Manuscript Submission

The *Journal of Affective Disorders* now proceeds totally online via an electronic submission system. Mail submissions will no longer be accepted. By accessing the online submission system through the Author Gateway, <http://ees.elsevier.com/jad/>, you will be guided stepwise through the creation and uploading of the various files. When submitting a manuscript online, authors need to provide an electronic version of their manuscript and any accompanying figures and tables.

The author should select from a list of scientific classifications, which will be used to help the editors select reviewers with appropriate expertise, and an article type for their manuscript. Once the uploading is done, the system automatically generates an electronic (PDF) proof, which is then used for reviewing. All correspondence, including the Editor's decision and request for revisions, will be processed through the system and will reach the corresponding author by e-mail.

Once a manuscript has successfully been submitted via the online submission system authors may track the status of their manuscript using the online submission system (details will be provided by e-mail). If your manuscript is accepted by the journal,

subsequent tracking facilities are available on Elsevier's Author Gateway, using the unique reference number provided by Elsevier and corresponding author name (details will be provided by e-mail).

Authors may send queries concerning the submission process or journal procedures to the appropriate Editorial Office:

For Europe, Asia (except Japan), and Australasia: C. Katona, Wingham Barton Manor, Westmarsh, Canterbury CT3 2LW, UK; E-mail: journalaffdis@googlemail.com.

For the American Hemisphere, Africa, and Japan: H.S. Akiskal, University of California at San Diego, V.A. Psychiatry Service (116A), 3350 La Jolla Village Dr., San Diego, CA 92161, USA; E-mail: hakiskal@ucsd.edu.

For further details on how to submit online, please refer to the online EES Tutorial for authors or contact Elsevier's Author Support Team at authorsupport@elsevier.com.

Types of Papers

The Journal primarily publishes

full-length Research Reports describing original work (4000-5000 words, excluding references and up to 6 tables/figures)

Brief Reports (1500-2000 words, excluding references and a maximum of 2 tables/figures)

evidence-based Review Articles (up to 8000 words, excluding references and up to 10 tables/figures). Reviews should be systematic and give details as to search strategy used.

Rapid Communications (1500-2000 words, excluding references and a maximum of 2 tables/figures).

Preliminary Communications (up to 3000 words, excluding references and maximum 3 tables/figures).

Books for review should be sent to the appropriate editorial office (see above).

At the discretion of the accepting Editor-in-Chief, and/or based on reviewer feedback, authors may be allowed fewer or more than these guidelines.

Preparation of Manuscripts

Articles should be in English. The title page should appear as a separate sheet bearing title (without article type), author names and affiliations, and a footnote with

the corresponding author's full contact information, including address, telephone and fax numbers, and e-mail address (failure to include an e-mail address can delay processing of the manuscript).

Papers should be divided into sections headed by a caption (e.g., Introduction, Methods, Results, Discussion). A structured abstract of no more than 250 words should appear on a separate page with the following headings and order: Background, Methods, Results, Limitations, Conclusions (which should contain a statement about the clinical relevance of the research). A list of three to six key words should appear under the abstract.

Authors should note that the 'limitations' section both in the discussion of the paper AND IN A STRUCTURED ABSTRACT are essential. Failure to include it may delay in processing the paper, decision making and final publication.

Ethical Considerations. Authors of reports on human studies, especially those involving placebo, symptom provocation, drug discontinuation, or patients with disorders that may impair decision-making capability, should consider the ethical issues related to the work presented and include (in the Methods and Materials section of their manuscript) detailed information on the informed consent process, including the method or methods used to assess the subject's capacity to give informed consent, and safeguards included in the study design for protection of human subjects. Specifically, authors should consider all ethical issues relevant to their research, and briefly address each of these in their reports. When relevant patient follow-up data are available, this should also be reported. Specifically, investigators reporting on research involving human subjects or animals must have prior approval from an institutional review board. This approval should be mentioned in the methods section of the manuscript. In countries where institutional review boards are not available; the authors must include a statement that research was conducted in accordance with the Helsinki Declaration as revised 1989. All studies involving animals must state that the authors followed the guidelines for the use and care of laboratory animals of the author's institution or the National Research Council or any national law pertaining to animal research care.

Author Disclosure

Funding body agreements and policies Elsevier has established agreements and developed policies to allow authors whose articles appear in journals published by Elsevier, to comply with potential manuscript archiving requirements as specified as conditions of their grant awards. To learn more about existing agreements and policies please visit <http://www.elsevier.com/fundingbodies>

The second aspect of the Journal's new policy concerns the **Conflict of Interest**. ALL authors are requested to disclose any actual or potential conflict of interest including any financial, personal or other relationships with other people or organizations within three (3) years of beginning the work submitted that could inappropriately influence, or be perceived to influence, their work.

Examples of potential conflicts of interest which should be disclosed include employment, consultancies, stock ownership (except for personal investment purposes equal to the lesser of one percent (1%) or USD 5000), honoraria, paid expert testimony, patent applications, registrations, and grants. If there are no conflicts of interest, authors should state that there are none.

e.g., Author Y owns shares in pharma company A. Author X and Z have consulted for pharma company B. All other authors declare that they have no conflicts of interest.

Finally, before the references, the Journal will publish **Acknowledgements**, in a separate section, and not as a footnote on the title page.

e.g., We thank Mr A, who kindly provided the data necessary for our analysis, and Miss B, who assisted with the preparation and proof-reading of the manuscript.

The submitting author is also required to make a brief statement concerning each named author's contributions to the paper under the heading **Contributors**. This statement is for editorial purposes only and will not be published with the article.

e.g., Author X designed the study and wrote the protocol. Author Y managed the literature searches and analyses. Authors X and Z undertook the statistical analysis, and author W wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

NB. During the online submission process the author will be prompted to **upload these four mandatory author disclosures as separate items**. They will be automatically incorporated in the PDF builder of the online submission system. **Please do not include in the main manuscripts.**

References

References should be cited in text by authors' names and year of publication (Harvard system). When referring to a work of more than two authors, the name of the first author should be used with 'et al.' (examples: Brown, 1992; Brown and Bifulco, 1992; Brown et al., 1993, a, b).

All references cited in text should be listed at the end of the paper (double spaced) arranged in alphabetical order of first author. More than one paper from the same author in the same year should be identified by the letter (a, b, c, etc.) after the year of publication.

The reference list should contain names and initials of all authors, year, title of paper referred to, abbreviated title of periodical (per Index Medicus), volume, and inclusive page numbers. This Journal should be cited in the list of references as J. Affect. Disord. Periodicals, books, and multi-author titles should accord with the following examples:

Bauer, M.S., Shea, N., McBride, L., Gavin, C., 1997. Predictors of service utilization in veterans with bipolar disorder: a prospective study. J. Affect. Disord. 44, 159-168.

Gelenberg, A.J., Bassuk, E.L., Schoonover, S.C., 1991. The Practitioner's Guide to Psychoactive Drugs. Plenum Medical Book Company, New York, NY.


Willner, P., 1995. Dopaminergic mechanisms in depression and mania. In: Bloom, F.E. and Kupfer, D.J. (Eds.), Psychopharmacology: The Fourth Generation of Progress. Raven Press, NY, pp. 921-931.

Figures and Photographs

Figures and Photographs of good quality should be submitted online as a separate file. Please use a lettering that remains clearly readable even after reduction to about 66%. For every figure or photograph, a legend should be provided. All authors wishing to use illustrations already published must first obtain the permission of the author and publisher and/or copyright holders and give precise reference to the original work. This permission must include the right to publish in electronic media.

Tables

Tables should be numbered consecutively with Arabic numerals and must be cited in the text in sequence. Each table, with an appropriate brief legend, comprehensible without reference to the text, should be typed on a separate page and uploaded online. Tables should be kept as simple as possible and wherever possible a graphical representation used instead. Table titles should be complete but brief. Information other than that defining the data should be presented as footnotes.

Please refer to the generic Elsevier artwork instructions:  <http://authors.elsevier.com/artwork/jad>.

Preparation of supplementary data

Elsevier accepts electronic supplementary material to support and enhance your scientific research. Supplementary files offer the author additional possibilities to publish supporting applications, movies, animation sequences, high-resolution images, background datasets, sound clips and more. Supplementary files supplied will be published online alongside the electronic version of your article in Elsevier web products, including ScienceDirect: <http://www.sciencedirect.com>. In order to ensure that your submitted material is directly usable, please ensure that data is provided in one of our recommended file formats. Authors should submit the material in electronic format together with the article and supply a concise and descriptive caption for each file. For more detailed instructions please visit our Author Gateway at: <http://www.elsevier.com/authors>

Colour reproduction

The *Journal of Affective Disorders* is now also included in a new initiative from Elsevier: 'Colourful e-Products'. Through this initiative, figures that appear in black & white in print can appear in colour, online, in ScienceDirect at <http://www.sciencedirect.com>.

There is no extra charge for authors who participate.

For colour reproduction in print, you will receive information regarding the costs from Elsevier after receipt of your accepted article. Please indicate your preference for colour in print or on the Web only. Because of technical complications which can arise by converting colour figures to "grey scale" (for the printed version should you not opt for colour in print) please submit in addition usable black and white versions of all the colour illustrations. For further information on the preparation of electronic artwork, please see <http://authors.elsevier.com/artwork/jad>.

Copyright Transfer

Upon acceptance of an article, you will be asked to transfer copyright (for more information on copyright see <http://authors.elsevier.com/journal/jad>). This transfer will ensure the widest possible dissemination of information. If excerpts from other copyrighted works are included in the submission, the author(s) must obtain written permission from the copyright owners and credit the source(s) in the article. Elsevier has preprinted forms for use by authors in these cases: contact Elsevier's Rights Department, Philadelphia, PA, USA: phone (+1) 215 238 7869, fax (+1) 215 238 2239, e-mail healthpermissions@elsevier.com.

Requests for materials from other Elsevier publications may also be completed on-

line via the Elsevier homepage <http://www.elsevier.com/locate/permissions>

Proofs

One set of proofs in PDF format will be sent by email to the corresponding Author, to be checked for typesetting/editing. No changes in, or additions to, the accepted (and subsequently edited) manuscript will be allowed at this stage. Proofreading is solely your responsibility. A form with queries from the copyeditor may accompany your proofs. Please answer all queries and make any corrections or additions required. The Publisher reserves the right to proceed with publication if corrections are not communicated. Return corrections within 2 days of receipt of the proofs. Should there be no corrections, please confirm this.

Elsevier will do everything possible to get your article corrected and published as quickly and accurately as possible. In order to do this we need your help. When you receive the (PDF) proof of your article for correction, it is important to ensure that all of your corrections are sent back to us in one communication. Subsequent corrections will not be possible, so please ensure your first sending is complete. Note that this does not mean you have any less time to make your corrections, just that only one set of corrections will be accepted.

Reprints

The corresponding author, at no cost, will be provided with a PDF file of the article via e-mail. The PDF file is a watermarked version of the published article and includes a cover sheet with the journal cover image and a disclaimer outlining the terms and conditions of use. There are no page charges.

Author enquiries For enquiries relating to the submission of articles please visit Elsevier's Author Gateway at <http://authors.elsevier.com/journal/jad>. The Author Gateway also provides the facility to track accepted articles and set up e-mail alerts to inform you of when an article's status has changed, as well as detailed artwork guidelines, copyright information, frequently asked questions and more. Contact details for questions arising after acceptance of an article, especially those relating to proofs, are provided after registration of an article for publication

Appendix 2 Systematic Review Database Search Terms

Embase Search Terms

- 1 cognition/ or attention/ or executive function/ or learning/ or memory/ or mental capacity/ or mental performance/ or orientation/ or social cognition/ or "theory of mind"/ or thinking/
- 2 neurocognition.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
- 3 exp task performance/ or exp attention/ or exp learning/ or exp cognition/
- 4 "inhibition (psychology)"/co [Complication]
- 5 inhibition.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
- 6 central coherence.mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
- 7 exp cognitive defect/
- 8 exp memory/ or exp short term memory/ or exp autobiographical memory/ or exp procedural memory/ or exp spatial memory/ or exp auditory memory/ or exp associative memory/ or exp tactile memory/ or exp working memory/ or exp visual memory/ or exp explicit memory/ or exp implicit memory/ or exp sensory memory/ or exp memory disorder/ or exp declarative memory/ or exp verbal memory/ or exp long term memory/ or exp semantic memory/ or exp episodic memory/
- 9 decision making.mp. or exp decision making/
- 10 exp motor control/
- 11 exp spatial discrimination/ or exp hemispheric dominance/ or exp task performance/
- 12 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
- 13 Neuropsychological test.mp. or exp neuropsychological test/
- 14 12 or 13
- 15 exp anxiety/ or exp anxiety neurosis/ or exp generalized anxiety disorder/ or exp anxiety disorder/ or exp "mixed anxiety and depression"/
- 16 exp panic/

17 exp agoraphobia/
18 exp social phobia/ or exp phobia/
19 exp posttraumatic stress disorder/
20 exp obsession/ or exp obsessive compulsive disorder/ or exp compulsion/
21 social anxiety.mp.
22 15 or 16 or 17 or 18 or 19 or 20 or 21
23 14 and 22
24 limit 23 to (english language and yr="1980 -Current")
25 13 and 24
26 limit 25 to adult <18 to 64 years>

Medline Search Terms

- 1 exp Cognition/ or exp Cognition Disorders/ or exp Neuropsychological Tests/ or neurocognition.mp.
- 2 attention.mp. or exp Attention/
- 3 exp Problem Solving/ or executive function.mp. or exp Executive Function/ or exp Mental Processes/
- 4 exp Association Learning/ or exp Learning/ or exp Paired-Associate Learning/ or learning.mp. or exp Discrimination Learning/ or exp Verbal Learning/
- 5 memory.mp. or exp Memory/ or exp Memory, Long-Term/ or exp Memory, Episodic/ or exp Memory Disorders/ or exp Memory, Short-Term/
- 6 exp Mental Competency/ or exp Decision Making/ or exp Mental Processes/ or mental capacity.mp. or exp Intelligence/
- 7 exp Psychomotor Performance/ or mental performance.mp.
- 8 orientation.mp. or exp Orientation/
- 9 exp Social Perception/ or social cognition.mp.
- 10 theory of mind.mp. or exp "Theory of Mind"/
- 11 thinking.mp. or exp Thinking/
- 12 task performance.mp. or exp "Task Performance and Analysis"/
- 13 inhibition.mp. or exp "Inhibition (Psychology)"/
- 14 central coherence.mp.
- 15 decision making.mp. or exp Decision Making/
- 16 exp Motor Skills/ or motor control.mp.
- 17 exp Visual Perception/ or exp Pattern Recognition, Visual/ or visuospatial processing.mp.
- 18 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
- 19 exp Anxiety/ or exp Anxiety Disorders/ or anxiety.mp.
- 20 generalised anxiety disorder.mp.
- 21 (mixed anxiety and depression).mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
- 22 exp Panic Disorder/ or exp Panic/ or panic.mp.
- 23 agoraphobia.mp. or exp Agoraphobia/
- 24 phobia.mp. or exp Phobic Disorders/
- 25 social anxiety.mp.
- 26 post traumatic stress disorder.mp. or exp Stress Disorders, Post-Traumatic/

- 27 obsessive compulsive disorder.mp. or exp Obsessive-Compulsive Disorder/
- 28 ocd.mp.
- 29 obsession.mp. or exp Obsessive Behavior/
- 30 exp Compulsive Behavior/ or compulsion.mp.
- 31 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
- 32 Neuropsychological test.mp. or exp Neuropsychological Tests/
- 33 18 and 31 and 32
- 34 limit 33 to (english language and yr="1980 -Current" and "all adult (19 plus
years)" and humans)
- 35 limit 34 to ("young adult and adult (19-24 and 19-44)" or "middle age (45 to 64
years)")

PsycInfo Search terms

- 1 exp Cognition/ or exp Cognition Disorders/ or exp Neuropsychological Tests/ or neurocognition.mp.
- 2 attention.mp. or exp Attention/
- 3 exp Problem Solving/ or executive function.mp. or exp Executive Function/ or exp Mental Processes/
- 4 exp Association Learning/ or exp Learning/ or exp Paired-Associate Learning/ or learning.mp. or exp Discrimination Learning/ or exp Verbal Learning/
- 5 memory.mp. or exp Memory/ or exp Memory, Long-Term/ or exp Memory, Episodic/ or exp Memory Disorders/ or exp Memory, Short-Term/
- 6 exp Mental Competency/ or exp Decision Making/ or exp Mental Processes/ or mental capacity.mp. or exp Intelligence/
- 7 exp Psychomotor Performance/ or mental performance.mp.
- 8 orientation.mp. or exp Orientation/
- 9 exp Social Perception/ or social cognition.mp.
- 10 theory of mind.mp. or exp "Theory of Mind"/
- 11 thinking.mp. or exp Thinking/
- 12 task performance.mp. or exp "Task Performance and Analysis"/
- 13 inhibition.mp. or exp "Inhibition (Psychology)"/
- 14 central coherence.mp.
- 15 decision making.mp. or exp Decision Making/
- 16 exp Motor Skills/ or motor control.mp.
- 17 exp Visual Perception/ or exp Pattern Recognition, Visual/ or visuospatial processing.mp.
- 18 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
- 19 exp Anxiety/ or exp Anxiety Disorders/ or anxiety.mp.
- 20 generalised anxiety disorder.mp.
- 21 (mixed anxiety and depression).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
- 22 exp Panic Disorder/ or exp Panic/ or panic.mp.
- 23 agoraphobia.mp. or exp Agoraphobia/
- 24 phobia.mp. or exp Phobic Disorders/
- 25 social anxiety.mp.
- 26 post traumatic stress disorder.mp. or exp Stress Disorders, Post-Traumatic/
- 27 obsessive compulsive disorder.mp. or exp Obsessive-Compulsive Disorder/

- 28 ocd.mp.
- 29 obsession.mp. or exp Obsessive Behavior/
- 30 exp Compulsive Behavior/ or compulsion.mp.
- 31 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30
- 32 Neuropsychological test.mp. or exp Neuropsychological Tests/
- 33 18 and 31 and 32
- 34 limit 33 to (human and english language and adulthood <18+ years> and
yr="1980 -Current")

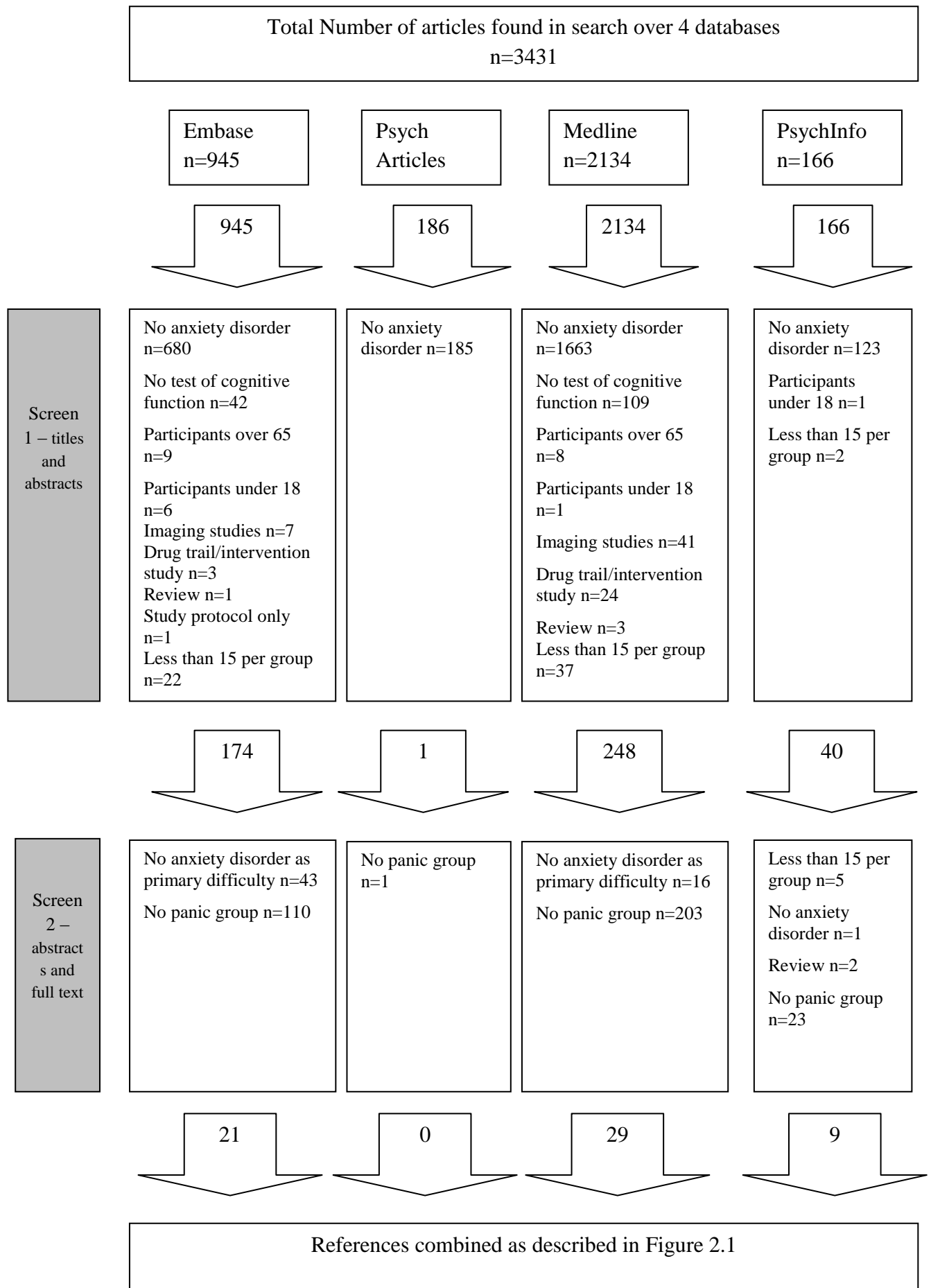
PsycArticles search terms

- 1 neurocognition.mp. [mp=title, abstract, full text, caption text]
- 2 cognition.mp. [mp=title, abstract, full text, caption text]
- 3 attention.mp. [mp=title, abstract, full text, caption text]
- 4 learning.mp. [mp=title, abstract, full text, caption text]
- 5 memory.mp. [mp=title, abstract, full text, caption text]
- 6 mental capacity.mp. [mp=title, abstract, full text, caption text]
- 7 executive function.mp. [mp=title, abstract, full text, caption text]
- 8 mental performance.mp. [mp=title, abstract, full text, caption text]
- 9 orientation.mp. [mp=title, abstract, full text, caption text]
- 10 social cognition.mp. [mp=title, abstract, full text, caption text]
- 11 thinking.mp. [mp=title, abstract, full text, caption text]
- 12 theory of mind.mp. [mp=title, abstract, full text, caption text]
- 13 task performance.mp. [mp=title, abstract, full text, caption text]
- 14 inhibition.mp. [mp=title, abstract, full text, caption text]
- 15 central coherence.mp. [mp=title, abstract, full text, caption text]
- 16 cognitive defect.mp. [mp=title, abstract, full text, caption text]
- 17 cognitive deficit.mp. [mp=title, abstract, full text, caption text]
- 18 decision making.mp. [mp=title, abstract, full text, caption text]
- 19 motor control.mp. [mp=title, abstract, full text, caption text]
- 20 visuospatial processing.mp. [mp=title, abstract, full text, caption text]
- 21 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16
or 17 or 18 or 19 or 20
- 22 Neuropsychological test.mp. [mp=title, abstract, full text, caption text]
- 23 anxiety.mp. [mp=title, abstract, full text, caption text]
- 24 anxiety disorder.mp. [mp=title, abstract, full text, caption text]
- 25 GAD.mp. [mp=title, abstract, full text, caption text]
- 26 (mixed anxiety and depression).mp. [mp=title, abstract, full text, caption text]
- 27 panic.mp. [mp=title, abstract, full text, caption text]
- 28 agoraphobia.mp. [mp=title, abstract, full text, caption text]
- 29 phobia.mp. [mp=title, abstract, full text, caption text]
- 30 social anxiety.mp. [mp=title, abstract, full text, caption text]
- 31 post traumatic stress disorder.mp. [mp=title, abstract, full text, caption text]
- 32 ptsd.mp. [mp=title, abstract, full text, caption text]
- 33 ocd.mp. [mp=title, abstract, full text, caption text]
- 34 obsessive compulsive disorder.mp. [mp=title, abstract, full text, caption text]

35 obsession.mp. [mp=title, abstract, full text, caption text]
36 compulsion.mp. [mp=title, abstract, full text, caption text]
37 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36

38 21 and 22 and 37
39 limit 38 to yr="1980 -Current"

Appendix 3 Detailed Search Diagram for Systematic Review



Appendix 4 Details of Quality Criteria

i. Eligibility criteria are specified

Well-covered (2)	Inclusion criteria clearly detailed and appropriate
Adequately addressed (1)	Inclusion criteria are not outlined clearly, though they can be ascertained from the details given.
Poorly addressed (0)	Some information is given about eligibility for the trial, though it could not be confidently replicated.
Not addressed (0)	

ii. Comparison group is matched

Well-covered (2)	A suitable comparison group is matched on age, gender, education or IQ
Adequately addressed (1)	Group only matched on some of the above.
Poorly addressed (0)	Not matched/ no details given
Not addressed (0)	

iii. Diagnosis using appropriate criteria and measure

Well-covered (2)	Diagnosis (or absence of diagnosis for HCs) ascertained by DSM/ICD criteria, structured interview by clinician
Adequately addressed (1)	Diagnosis by DSM/ICD criteria, using questionnaire based on DSM/ICD criteria
Poorly addressed (0)	Unspecified diagnosis procedure or questionnaire not specifically designed to reflect diagnostic criteria
Not addressed (0)	

iv. Neuropsychological Measures are robust

Well-covered (2)	Outcome measures robust for this population (valid, reliable) reliability and validity specified in paper or easily obtainable using Lezak et al.'s (2004) reference text or reference provided in the paper.
Adequately addressed (1)	Tests well described but reliability and validity not found as described in under 'well covered'. or Tests well described with reliability and validity given but not the most valid for this population
Poorly addressed (0)	Outcome measures poorly described and less robust.
Not addressed (0)	

v. Sample size adequate for all groups

Well-covered (2)	Sample size 25 or more in each group because of minimum number needed to detect large sample size
Adequately addressed (1)	Sample size 15-25 in each group
Poorly addressed (0)	Sample size not adequate (less than 15)
Not addressed (0)	

vi. Levels of uptake are reported

Well-covered (2)	Levels of uptake are reported and affects of uptake levels considered
Adequately addressed (1)	Levels of uptake described in detail
Poorly addressed (0)	Levels of uptake not described
Not addressed (0)	

vii. Results – appropriate outputs provided

Well-covered (2)	Means, standard deviations and confidence intervals reported
Adequately addressed (1)	Enough reported to facilitate comparison, not all of the above
Poorly addressed (0)	Some of above reported but not enough to make a complete comparison, or Selective reporting of initial measures mentioned in methods.
Not addressed (0)	

viii. Appropriate Statistical techniques

Well-covered (2)	Appropriate statistics used, compensations for multiple comparisons, new alpha level clearly stated.
Adequately addressed (1)	No corrections for multiple comparisons but otherwise adequate statistics used.
	Questionable statistics used - Post hoc tests used after a MANOVA or a variable used as a covariate where group differences exist on that variable
Poorly addressed (0)	Inappropriate statistics used
Not addressed (0)	

Appendix 5 Author Guidelines for Journal of the International Neuropsychological Society

Manuscript Length

In order to increase the number of manuscripts that can be published in the *JINS*, please adhere to the following length requirements. Please provide a word count on the title page for abstract and for manuscript (not including abstract, tables, figures, or references).

Manuscripts will be returned if they exceed length requirements.

Regular Research Articles: Maximum of 5,000 words (not including tables, figures, or references) and a 200 word abstract.

Manuscript Preparation and Style

The entire manuscript should be typed double-spaced throughout using any word processing program. Unless otherwise specified, the guideline for preparation of manuscripts is the *Publication Manual of the American Psychological Association* (6th edition). This may be ordered from: APA Order Dept., 750 1st St. NE, Washington, DC 20002-4242, USA.

Pages should be numbered sequentially beginning with the Title Page. The Title Page should contain the full title of the manuscript, the full names and affiliations of all authors, a contact address with telephone and fax numbers and e-mail address, and the word count for abstract and for manuscript (excluding title page, abstract, references, tables, and figures). At the top right provide a short title of up to 45 characters preceded by the lead author's last name. Example: Smith-Memory in Parkinson's Disease. This running headline should be repeated at the top right of every following page.

The Abstract and Mesh terms (Keywords) on *page 2* should include a brief statement of the problem, the method, the key findings, and the conclusions. Six mesh or key words should be provided (see <http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=mesh> for list), and they should not duplicate words in the title.

The full text of the manuscript should begin on *page 3*. For scientific articles, including *Regular Research Articles*, *Brief Communications*, *Rapid Communications*, and *Symposia*, the format should include an Abstract, Introduction,

Method, Results, and Discussion. This should be followed by References, Appendixes, Acknowledgments, Tables, Figures, and Figure Legends.

The use of abbreviations, except those that are widely used, is strongly discouraged. They should be used only if they contribute to better comprehension of the manuscript. Acronyms should be spelled out at first mention. Metric system (SI) units should be used.

Special Note Regarding Figures

Please upload your figure(s) in either a .doc or pdf. format. When uploading figures (colour or black and white), they need only be a high enough resolution for the reviewers and editors to identify the information you are trying to convey. However, if your manuscript is accepted for publication, your figures must meet the following criteria:

High quality digital images (600 dpi or higher) should be provided in PDF, EPS, or TIFF formats. If a digital image is not available, please scan in the image. Figures should be numbered consecutively as they appear in the text. Any indication of features of special interest should also be included. Figures should be twice their intended final size and authors should do their best to construct figures with notation and data points of sufficient size to permit legible photo reduction to one column of a two-column format.

Colour figures can be accepted. All colour graphics must be formatted in CMYK and not in RGB, because 4-color separations cannot be done in RGB. However, the extra cost of printing these figures must be paid by the author: \$500 for the first colour page, \$250 for each colour page thereafter.

Tables and figures should be numbered in Arabic numerals. The approximate position of each table and figure should be provided in the manuscript: [INSERT TABLE 1 HERE]. Tables and figures should be on separate pages. Tables should have short titles and all figure legends should be on separate pages.

If you plan to use figures or tables that have been redrawn or modified from other publications, and you are not the copyright holder, please obtain permission for this re-use. Authors should err on the side of caution and seek advice from the editorial office if they are uncertain whether to seek permission.

Financial Support

Please provide details of the sources of financial support for all authors, including grant numbers. For example, “This work was supported by the National Institutes of Health (grant number XXXXXXXX)”. Multiple grant numbers should be separated by a comma and space, and where research was funded by more than one agency the different agencies should be separated by a semi-colon, with “and” before the final funder. Grants held by different authors should be identified as belonging to individual authors by the authors’ initials. For example, “This work was supported by the Wellcome Trust (A.B., grant numbers XXXX, YYYY), (C.D., grant number ZZZZ); the Natural Environment Research Council (E.F., grant

number FFFF); and the National Institutes of Health (A.B., grant number GGGG), (E.F., grant number HHHH).” Where no specific funding has been provided for research, please provide the following statement “This research received no specific grant from any funding agency, commercial or not-for-profit sectors.”

References

References should be in American Psychological Association, 6th Edition, style (see the examples presented below).

Text references should be cited as follows: “. . . Given the critical role of the prefrontal cortex (PFC) in working memory (Cohen et al., 1997; Goldman-Rakic, 1987; Perlstein et al., 2003a, 2003b) . . .” with multiple references in alphabetical order. Another example is: “For example, Cohen et al. (1994,1997), Braver et al. (1997), and Jonides and Smith (1997) demonstrated . . .”

References cited in the text with two authors should list both names. References cited in the text with three, four, or five authors, list all authors at first mention; with subsequent citations, include only the first author’s last name followed by et al. References cited in the text with six or more authors should list the first author et al. throughout. In the reference section, list all authors up to seven. For eight or more, list the first six, then three ellipses, and end with the last author’s name. Examples of the APA reference style are as follows:

Online/Electronic Journal Article with DOI:

Dikmen, S., Machamer, J. Fann, J. & Temkin, N. (2010). Rates of Symptom Reporting Following Traumatic Brain Injury. *Journal of the International Neuropsychological Society*, 16, 401-411. doi: 10.1017/S1355617710000196

Scientific Article:

Haaland, K.Y., Price, L., & LaRue, A. (2003). What does the WMS-III tell us about memory changes with normal aging? *Journal of the International Neuropsychological Society*, 9, 89-96.

Book:

Lezak, M.D., Howieson, D.B., & Loring, D.W. (2004). *Neuropsychological Assessment*. New York: Oxford University Press.

Book Chapter:

Knopman, D. & Selnes, O. (2003). Neuropsychology of Dementia. In K.M. Heilman & E.E. Valenstein (Ed.), *Clinical Neuropsychology*. New York: Oxford University Press.

Report at a Scientific Meeting:

Rothi, L.J.G. (2003, February). Use-dependent learning and neural plasticity: A revision of the pessimism surrounding neurorehabilitation. International Neuropsychological Society, Honolulu, Hawaii.

Manual, Diagnostic Scheme, etc.:

American Psychiatric Association (1994). *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.). Washington, DC: American Psychiatric Association Press.

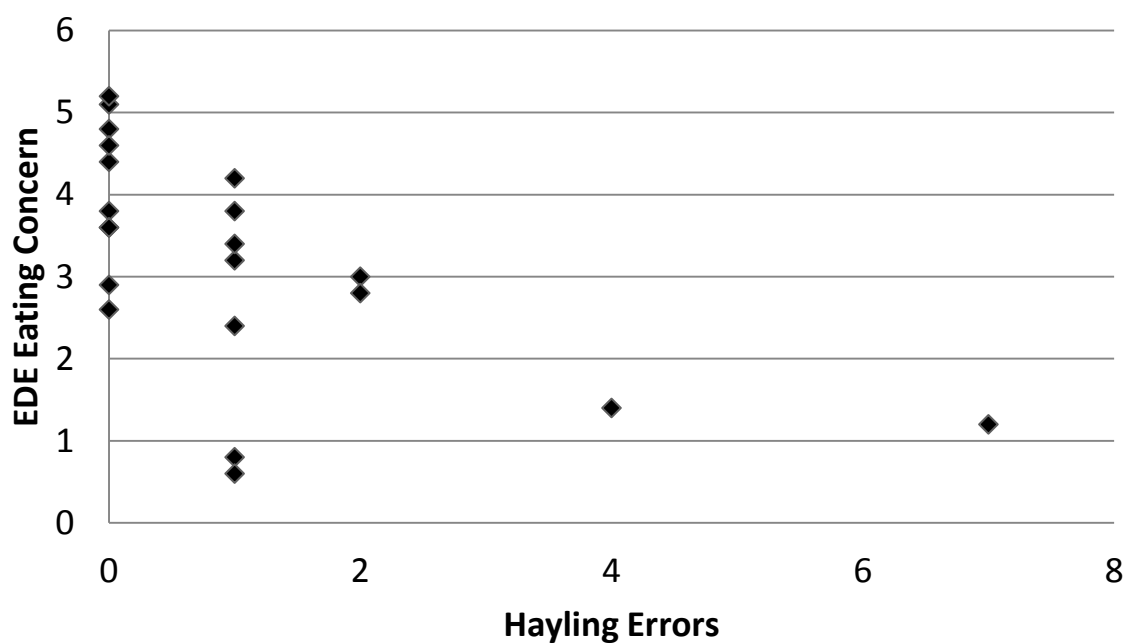
Proofs

The publisher reserves the right to copyedit manuscripts. The corresponding author will receive PDFs for final proofreading. These should be checked and corrections returned within 2 days of receipt. The publisher reserves the right to charge authors for excessive corrections.

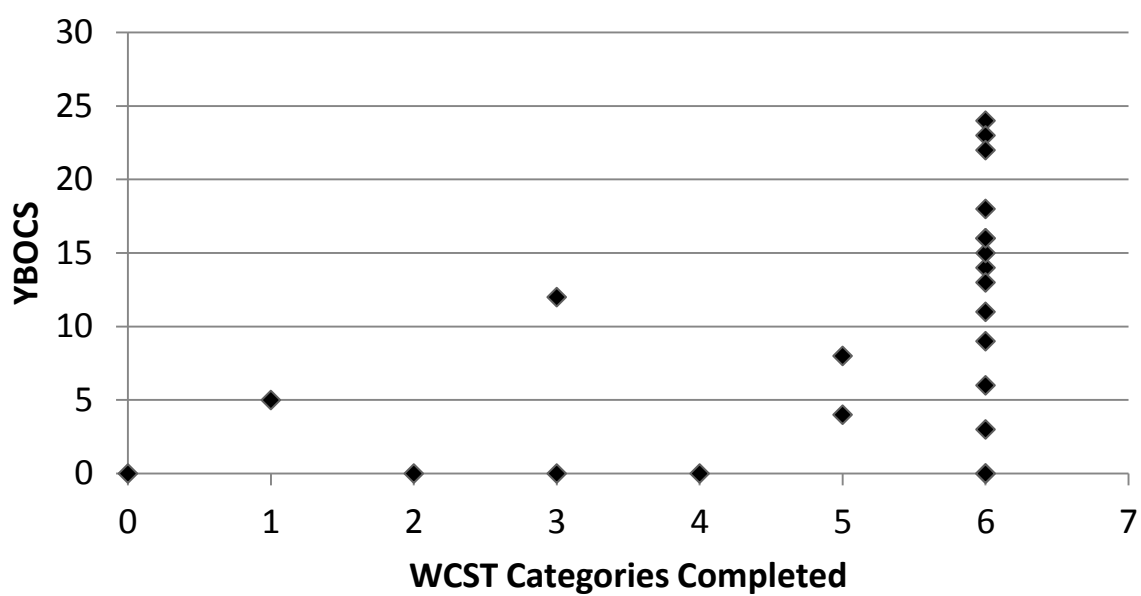
Offprints and PDF Files

The corresponding author will receive a free pdf. This pdf can also be mounted on the authors' web pages. Offprints must be ordered when page proofs are returned. The offprint order form with the price list will be sent with your PDF.

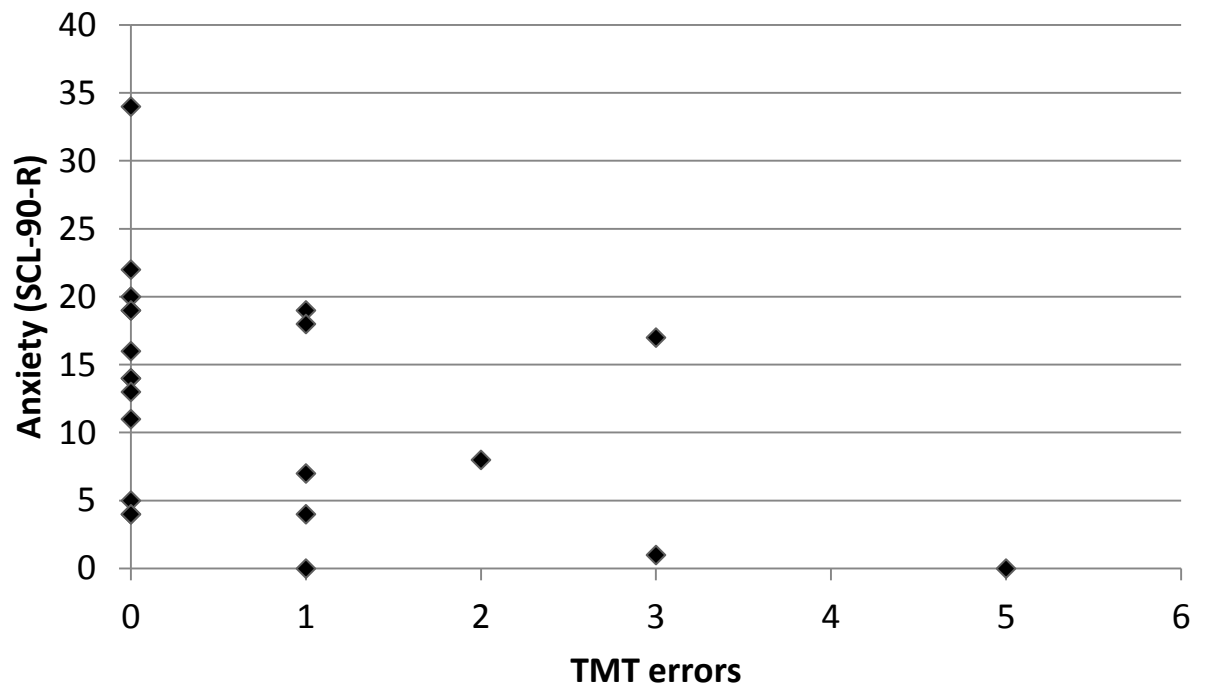
EDE Eating Concern and Hayling Errors in BN group



YBOCS and WCST categories completed in the AD group

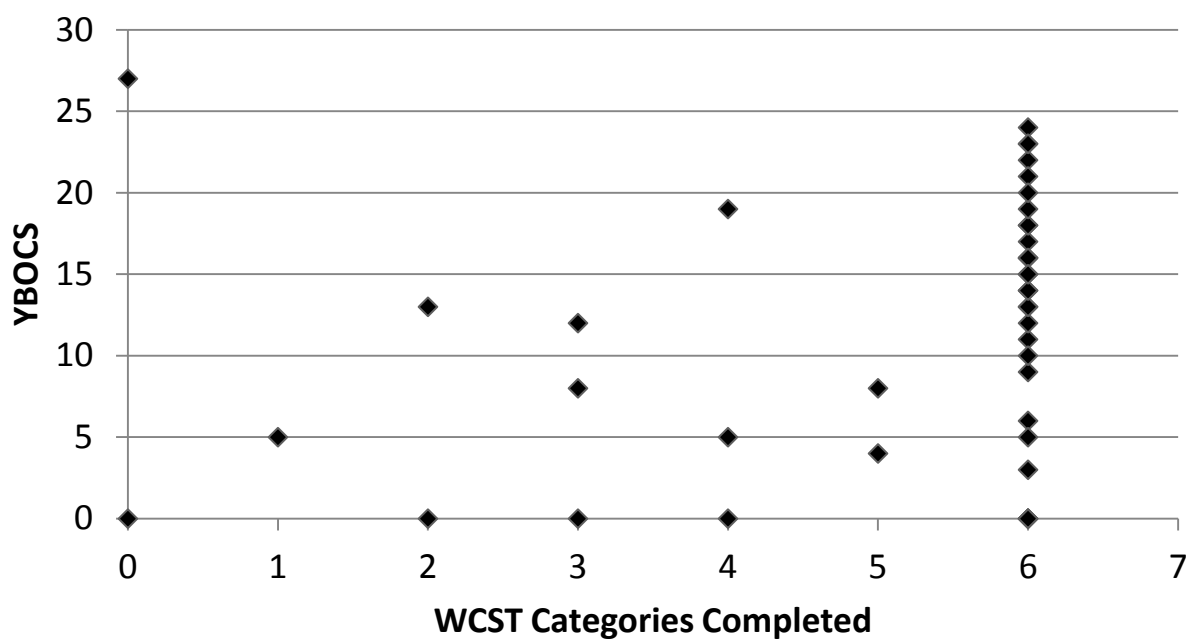


Anxiety (SCL-90-R) and TMT errors in AD group

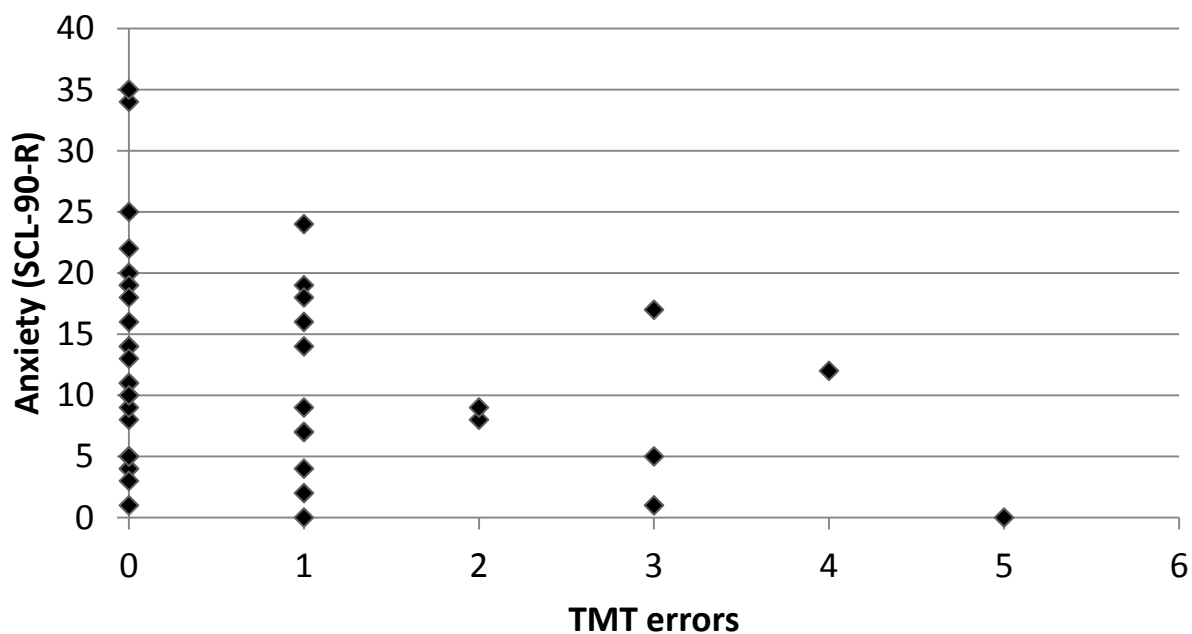


Relating to Section 4.3.3 – Both groups combined

YBOCS and WCST Categories Completed in Combined group



TMT errors and Anxiety (SCL-90-R) in Combined Groups



Appendix 7 Invitation letter to NHS Grampian Participants

Dear ,

I am writing to you as someone who is currently waiting for treatment for Bulimia with the NHS Grampian Eating Disorders Service. The service is currently supporting a research project investigating how people think and solve problems, as well as their flexibility when they are suffering from bulimia or atypical bulimia. This is being run in conjunction with colleagues from NHS Tayside.

Participation involves meeting with a researcher at the Eating Disorder Service at the Royal Cornhill Hospital and completing some brief neuropsychological pen-and-paper tasks which assess this flexibility. Some general feedback would be available on the outcome of these tasks. Participation would also involve gathering information about your current psychological symptoms through interview and questionnaires.

The project will run until the end of June. I have enclosed a leaflet with further information. If you have an interest in participating in the project or would like additional information please contact my colleagues Kate O'Sullivan or Jan Templeton whose details are listed below.

Yours sincerely,

Dr Phil Crockett

For further information contact:

Jan Templeton
Clinical Associate in Applied Psychology
Eating Disorder Service
Royal Cornhill Hospital
Tel: 01224 557 392 (main office)

Kate O'Sullivan
Trainee Clinical Psychologist
TSMS
Constitution House
Dundee
DD1 1LB
Tel: 0750 307 3108

Appendix 8 Participant Information Sheets

Eating disorder service Participant Information Sheet

Participant Information Sheet: NHS Grampian and NHS Tayside Eating Disorder Services

Neuropsychological Correlates of Eating Disorders in Adult Females

You are being invited to take part in a research study. We believe it to be of potential importance. Before you decide whether or not you wish to participate, we would like to explain why the study is being carried out, and what taking part will involve for you. Please read the following information carefully. If you have any questions please contact either of the people named at the bottom of this sheet, who will be happy to discuss the study and provide further information.

Background to the Study

Investigation of brain functioning in eating disorders is a relatively new field, however it is widely recognised as having potential to advance our understanding of eating disorders. Many aspects of brain functioning have been investigated in eating disorder populations including general intelligence, attention, memory, learning, visuospatial processing, and executive functioning. “Executive functioning” refers to a set of skills which include problem solving, planning, organisation, shifting attention, and decision making. There is evidence to suggest aspects of executive functioning may be impaired in this population. However it is not known how these impairments may affect individuals and their relationship to psychological characteristics commonly seen in people with eating disorders.

It is hoped this study will advance our understanding of eating disorders and help inform new interventions.

Why have I been chosen?

The study aims to compare individuals with bulimia nervosa, and other eating disorders to a clinical and a non-clinical comparison group. You are being asked to participate as part of a clinical group, as you are receiving treatment for an eating disorder in NHS Tayside or NHS Grampian. Everyone meeting certain criteria attending NHS Eating Disorder Services in Tayside or Grampian may be asked to consider taking part in the study.

Do I have to take part?

It is entirely your decision as to whether or not you take part in the study. If you decide to take part, you may withdraw at any time, without giving a reason. Equally, you may choose not to take part at all. **Your decision to take part or not, and the answers that you give will not influence any treatment that you are currently being given or may receive in the future.**

What does taking part involve?

If you decide you would like to take part in the study, you should let your clinician know, and they will pass your details on to a member of the research team to arrange a meeting. During the meeting you will be given the opportunity to ask questions about the study and then if you wish to proceed to complete a consent form. The investigator will interview you about your eating behaviour and collect some basic information. The investigator will then administer a range of neuropsychological tests. These are similar to tests seen on “brain training” games and involve problem solving and pen and paper tasks. This will take approximately 45-60 minutes. You will then be given a short break before being asked to fill in 4 questionnaires. In total this will take about 1.5-2 hours. After participation in the study you will have the opportunity for discussion with the investigator and get general feedback about your neuropsychological test performance. The treatment you will receive if you do take part in the study will be no different from the treatment you would receive otherwise.

What are the possible disadvantages and advantages of taking part?

The study will take approximately 1.5-2 hours to complete, which you may find an inconvenience. The questions and tests administered are the same for every participant, and are not intended to reflect any personal causes of eating disorders however some of the questions asked during interview or in the questionnaires may give rise to difficult feelings. The investigator will be available to discuss any issues that may arise during participation, and can direct you to internal and external sources of support. After participation you will have a discussion with the investigator and get general feedback about your neuropsychological test performance, which may be of interest. It is hoped that the information gathered will be of value in enhancing our understanding of eating disorders and in informing new interventions.

Will my taking part in the study be confidential?

Participation in the study is completely confidential. Confidentiality may be limited if there is an issue of risk to yourself or others, in which instance the investigator may contact her supervisor Dr Alison Livingston and clinical staff within the relevant Eating Disorder Service may be informed.

Has this study been ethically reviewed?

The study has been reviewed by The University of Edinburgh’s School of Health ethics committee and The University of Stirling Psychology Department ethics committee. It has been approved through NHS Tayside Research Ethics Committee and NHS Tayside Research and Development Department.

How can I make a complaint about this study?

If you believe that you have been harmed in any way by taking part in the study you have the right to pursue a complaint and seek any resulting compensation through the usual NHS process. To do so you can submit a written complaint to the Patient Liaison Manager, Complaints Office, Ninewells Hospital (Freephone 0800 027 5507). Note that the NHS has no legal liability for non-negligent harm. However if

you are harmed and this is due to someone's negligence, you may have grounds for a legal action against NHS Tayside but you may have to pay your legal costs.

Contact Details

If you would like more information on the study or have any questions, please contact:

Kate O'Sullivan,
Trainee Clinical Psychologist
Email: kate.osullivan@nhs.net;
Tel: 01382 306150

Dr Alison Livingstone,
Consultant Clinical Neuropsychologist & Lead
Clinician,
Department of Clinical Neuropsychology,
Level 6, Ninewells Hospital, Dundee, DD1 9SY.
01382 740 406
Email: alison.livingstone@nhs.net

Thank you for taking the time to read this information sheet.



Participant Information Sheet: NHS Tayside Psychological Therapies Service
Neuropsychological Correlates of Eating Disorders in Adult Females

You are being invited to take part in a research study. We believe it to be of potential importance. Before you decide whether or not you wish to participate, we would like to explain why the study is being carried out, and what taking part will involve for you. Please read the following information carefully. If you have any questions please contact either of the people named at the bottom of this sheet, who will be happy to discuss the study and provide further information.

Background to the Study

Anxiety and depression are often comorbid with eating disorders. Investigation of brain functioning in eating disorders is a relatively new field, however it is widely recognised as having potential to advance our understanding of eating disorders. Since anxiety and depression can also affect brain functioning, they need to be taken into account when we investigate brain function in eating disorders. Many aspects of brain functioning have been investigated in eating disorder populations including general intelligence, attention, memory, learning, visuospatial processing, and executive functioning. “Executive functioning” refers to a set of skills which include problem solving, planning, organisation, shifting attention, and decision making. There is evidence to suggest aspects of executive functioning may be impaired in this population. However it is not known how these impairments may affect individuals and their relationship to psychological characteristics commonly seen in people with eating disorders.

This study aims to investigate executive function in eating disorders and account for comorbidity by also studying a clinical comparison group of age and gender matched individuals with anxiety and/or depression. It is hoped this study will advance our understanding of eating disorders and help inform new interventions.

Why have I been chosen?

The study aims to compare individuals with bulimia nervosa, and other eating disorders to a clinical and a non-clinical comparison group. You are being asked to participate as part of a clinical comparison group, as you are receiving treatment in NHS Tayside Adult Psychological Therapies Service. Everyone meeting certain criteria attending NHS Tayside Adult Psychological Therapies Service may be asked to consider taking part in the study.

Do I have to take part?

It is entirely your decision as to whether or not you take part in the study. If you decide to take part, you may withdraw at any time, without giving a reason. Equally, you may choose not to take part at all. **Your decision to take part or not, and the answers that you give will not influence any treatment that you are currently being given or may receive in the future.**

What does taking part involve?

If you decide you would like to take part in the study, you should let your clinician know, and they will pass your details on to a member of the research team to arrange a meeting. During the meeting you will be given the opportunity to ask questions about the study and then if you wish to proceed to complete a consent form. The investigator will interview you about your eating behaviour and collect some basic information. The investigator will then administer a range of neuropsychological tests. These are similar to tests seen on “brain training” games and involve problem solving and pen and paper tasks. This will take approximately 45-60 minutes. You will then be given a short break before being asked to fill in 4 questionnaires. In total this will take about 1.5-2 hours. After participation in the study you will have the opportunity for discussion with the investigator and get general feedback about your neuropsychological test performance. The treatment you will receive if you do take part in the study will be no different from the treatment you would receive otherwise.

What are the possible disadvantages and advantages of taking part?

The study will take approximately 1.5-2 hours to complete, which you may find an inconvenience. The questions and tests administered are the same for every participant, and are not intended to reflect any personal causes of eating disorders however some of the questions asked during interview or in the questionnaires may give rise to difficult feelings. The investigator will be available to discuss any issues that may arise during participation, and can direct you to internal and external sources of support. After participation you will have a discussion with the investigator and get general feedback about your neuropsychological test performance, which may be of interest. It is hoped that the information gathered will be of value in enhancing our understanding of eating disorders and in informing new interventions.

Will my taking part in the study be confidential?

Participation in the study is completely confidential. Confidentiality may be limited if there is an issue of risk to yourself or others, in which instance the investigator may contact her supervisor Dr Alison Livingston and clinical staff within NHS Tayside Adult Psychological Therapies Services may be informed.

Has this study been ethically reviewed?

The study has been reviewed by The University of Edinburgh's School of Health ethics committee and The University of Stirling Psychology Department ethics committee. It has been approved through NHS Tayside Research Ethics Committee and NHS Tayside Research and Development Department.

How can I make a complaint about this study?

If you believe that you have been harmed in any way by taking part in the study you have the right to pursue a complaint and seek any resulting compensation through the usual NHS process. To do so you can submit a written complaint to the Patient Liaison Manager, Complaints Office, Ninewells Hospital (Freephone 0800 027 5507). Note that the NHS has no legal liability for non-negligent harm. However if you are harmed and this is due to someone's negligence, you may have grounds for a legal action against NHS Tayside but you may have to pay your legal costs.

Contact Details

If you would like more information on the study or have any questions, please contact:

Kate O'Sullivan,
Trainee Clinical Psychologist
Email: kate.osullivan@nhs.net;
Tel: 01382 306150

Dr Alison Livingstone,
Consultant Clinical Neuropsychologist & Lead
Clinician,
Department of Clinical Neuropsychology,
Level 6, Ninewells Hospital, Dundee, DD1 9SY.
01382 740 406
Email: alison.livingstone@nhs.net

Thank you for taking the time to read this information sheet.

Participant information Sheet for Bulimic Patients in the Adult Psychological
Therapies Service (Never Used)



Participant Information Sheet: NHS Tayside Psychological Therapies Service
Neuropsychological Correlates of Eating Disorders in Adult Females

You are being invited to take part in a research study. We believe it to be of potential importance. Before you decide whether or not you wish to participate, we would like to explain why the study is being carried out, and what taking part will involve for you. Please read the following information carefully. If you have any questions please contact either of the people named at the bottom of this sheet, who will be happy to discuss the study and provide further information.

Background to the Study

Investigation of brain functioning in eating disorders is a relatively new field, however it is widely recognised as having potential to advance our understanding of eating disorders. Many aspects of brain functioning have been investigated in eating disorder populations including general intelligence, attention, memory, learning, visuospatial processing, and executive functioning. “Executive functioning” refers to a set of skills which include problem solving, planning, organisation, shifting attention, and decision making. There is evidence to suggest aspects of executive functioning may be impaired in this population. However it is not known how these impairments may affect individuals and their relationship to psychological characteristics commonly seen in people with eating disorders.

It is hoped this study will advance our understanding of eating disorders and help inform new interventions.

Why have I been chosen?

The study aims to compare individuals with bulimia nervosa, and other eating disorders to a clinical and a non-clinical comparison group. You are being asked to participate as part of a clinical group, as you are receiving treatment for an eating disorder in NHS Tayside. Everyone meeting certain criteria attending NHS Tayside Adult Psychological Therapies Service may be asked to consider taking part in the study.

Do I have to take part?

It is entirely your decision as to whether or not you take part in the study. If you decide to take part, you may withdraw at any time, without giving a reason. Equally, you may choose not to take part at all. **Your decision to take part or not, and the**

answers that you give will not influence any treatment that you are currently being given or may receive in the future.

What does taking part involve?

If you decide you would like to take part in the study, you should let your clinician know, and they will pass your details on to a member of the research team to arrange a meeting. During the meeting you will be given the opportunity to ask questions about the study and then if you wish to proceed to complete a consent form. The investigator will interview you about your eating behaviour and collect some basic information. The investigator will then administer a range of neuropsychological tests. These are similar to tests seen on “brain training” games and involve problem solving and pen and paper tasks. This will take approximately 45-60 minutes. You will then be given a short break before being asked to fill in 4 questionnaires. In total this will take about 1.5-2 hours. After participation in the study you will have the opportunity for discussion with the investigator and get general feedback about your neuropsychological test performance. The treatment you will receive if you do take part in the study will be no different from the treatment you would receive otherwise.

What are the possible disadvantages and advantages of taking part?

The study will take approximately 1.5-2 hours to complete, which you may find an inconvenience. The questions and tests administered are the same for every participant, and are not intended to reflect any personal causes of eating disorders however some of the questions asked during interview or in the questionnaires may give rise to difficult feelings. The investigator will be available to discuss any issues that may arise during participation, and can direct you to internal and external sources of support. After participation you will have a discussion with the investigator and get general feedback about your neuropsychological test performance, which may be of interest. It is hoped that the information gathered will be of value in enhancing our understanding of eating disorders and in informing new interventions.

Will my taking part in the study be confidential?

Participation in the study is completely confidential. Confidentiality may be limited if there is an issue of risk to yourself or others, in which instance the investigator may contact her supervisor Dr Alison Livingston and clinical staff within NHS Tayside Adult Psychological Therapies Services may be informed.

Has this study been ethically reviewed?

The study has been reviewed by The University of Edinburgh’s School of Health ethics committee and The University of Stirling Psychology Department ethics

committee. It has been approved through NHS Tayside Research Ethics Committee and NHS Tayside Research and Development Department.

How can I make a complaint about this study?

If you believe that you have been harmed in any way by taking part in the study you have the right to pursue a complaint and seek any resulting compensation through the usual NHS process. To do so you can submit a written complaint to the Patient Liaison Manager, Complaints Office, Ninewells Hospital (Freephone 0800 027 5507). Note that the NHS has no legal liability for non-negligent harm. However if you are harmed and this is due to someone's negligence, you may have grounds for a legal action against NHS Tayside but you may have to pay your legal costs.

Contact Details

If you would like more information on the study or have any questions, please contact:

Kate O'Sullivan,
Trainee Clinical Psychologist
Email: kate.osullivan@nhs.net;
Tel: 01382 306150

Dr Alison Livingstone,
Consultant Clinical Neuropsychologist & Lead
Clinician,
Department of Clinical Neuropsychology,
Level 6, Ninewells Hospital, Dundee, DD1 9SY.
01382 740 406
Email: alison.livingstone@nhs.net

Thank you for taking the time to read this information sheet.

Appendix 9 Letters of Ethical Approval

Approval of Substantial amendment to Tayside Eating Disorder Research Group existing approval.

East of Scotland Research Ethics Service

Tayside Committee on Medical Research Ethics A
Research Ethics Office
Tayside Academic Health Sciences Centre
Ninewells Hospital & Medical School
Residency Block, Level 3
George Pirie Way
Dundee
DD1 9SY

Dr Alison Livingstone
Department of Clinical Neuropsychology
Level 6, South Block
Ninewells Hospital & Medical School
Dundee
DD1 9SY

Date: 29 September 2011
Your Ref:
Our Ref: LR/08/S1401/133
Enquiries to: Mrs Loraine Reilly
Extension: Ninewells extension 40099
Direct Line: 01382 740099
Email: loraine.reilly@nhs.net

Dear Dr Livingstone

Study title: Neuropsychological Correlates of Eating Disorders in Adult Females
REC reference: 08/S1401/133
Amendment number: AM06 (For REC Reference Only)
Amendment date: 24 September 2011

The above amendment was reviewed at the meeting of the Sub-Committee held on 29 September 2011.

Ethical opinion

There were no ethical issues noted.

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
CV - Professor Kevin G. Power		
CV - Ms Kate O'Sullivan		26 September 2011
CV - Mrs Alison Peaker		
Electronic Form: Patient Contact Details	1	24 September 2011
Description of new sites: Group 4 & 5	1	24 September 2011
Group 5 Inclusion/Exclusion Criteria	1	24 September 2011
Questionnaire: Group 5 Anxious/Depressed Patients	1	24 September 2011
Questionnaire: Group 4 Bulimia	2	24 September 2011
Participant Information Sheet: Group 5 Comparison Group	1	24 September 2011
Participant Information Sheet: Group 4 Bulimic Group	2	24 September 2011
Participant Information Sheet: Group 5 Anxious and/or	1	24 September 2011

Depressed Patients		
Participant Information Sheet: Group 4 Bulimic Patients for Adult Services	2	24 September 2011
Participant Information Sheet: Group 4 Bulimic Patients form Eating Disorder Services	2	24 September 2011
Protocol	5	24 September 2011
Notice of Substantial Amendment (non-CTIMPs)	AM06	24 September 2011
Covering Letter		27 September 2011
Details of Local Collaborator		

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.


Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

08/S1401/133:

Please quote this number on all correspondence

Yours sincerely


for **Dr Fergus Daly**
Alternate Vice-chair

Email: lorraine.reilly@nhs.net

Enclosures: List of names and professions of members who were present at the meeting and those who submitted written comments

Copy to: Ms Elspeth Currie, Edinburgh Clinical Trials Unit
NHS Tayside R&D Office



Tayside Committee on Medical Research Ethics A

Attendance at Sub-Committee of the REC meeting on 29 September 2011

Committee Members:

Name	Profession	Present	Notes
Dr Fergus Daly	Clinical Trial Manager	Yes	Alternate Vice-chair
Mr John Macleod		Yes	

Also in attendance:

Name	Position (or reason for attending)
Mrs Lorraine Reilly	Co-ordinator



Research and Development Foresterhill House Annexe
Foresterhill
Aberdeen
AB25 2ZB

Dr Philip Crockett	Date	29 February 2012
Consultant Psychiatrist	Our Ref	2009PC006
in Eating Disorders	Enquiries to	Anne-Marie Sinclair
Eating Disorder Service	Extension	53846
Royal Cornhill Hospital	Direct Line	01224 553846
Aberdeen	Email	grampian.randdpermissions@nhs.net
AB25 2ZH		

Dear Dr Crockett

Project Title: Neuropsychological correlates of Anorexia Nervosa in Adult Females

Amendment no: AM06

Amendment date: 24/09/2011

Ethics ref: 08/S1401/133

Thank you for sending a copy of the amendment to the above project relating to changes to the Electronic Form: Patient Contact Details (v1, 24/09/2011), Description of new sites: Group 4 & 5 (v1, 24/09/2011), Group 5 Inclusion/Exclusion Criteria (v1, 24/09/2011), Questionnaire: Group 5 Anxious/Depressed Patients (v1, 24/09/2011), Questionnaire: Group 4 Bulimia (v2, 24/09/2011), Participant Information Sheet: Group 5 Comparison Group (v1, 24/09/2011), Participant Information Sheet: Group 4 Bulimic Group (v2, 24/09/2011), Participant Information Sheet: Group 5 Anxious and/or Depressed Patients (v1, 24/09/2011), Participant Information Sheet: Group 4 Bulimic Patients for Adult Services (v2, 24/09/2011), Participant Information Sheet: Group 4 Bulimic Patients from Eating Disorder Services (v2, 24/09/2011), Protocol (v5, 24/09/2011) and Details of Local Collaborator.

This letter is confirmation that this amendment does not alter local NHS Grampian R & D management permission of the project.

Yours sincerely

A handwritten signature in black ink, appearing to read 'S. Ridge', with a stylized flourish at the end.

Susan Ridge
Non Commercial Manager

Cc Dr Alison Livingstone, Consultant Clinical Neuropsychologist/ Lead Clinician,
NHS Tayside
Kate O'Sullivan, Trainee Clinical Psychologist, NHS Tayside

Ethical Approval for Original Study submission not including the groups used in the current study.



Fife



Forth Valley



Tayside

Fife, Forth Valley & Tayside Research Ethics Service

Tayside Committee on Medical Research Ethics A

Research Ethics Office

Level 9

Ninewells Hospital & Medical School

DUNDEE

DD1 9SY

Ms Helen Swanson
Department of Clinical Neuropsychology
Level 6
South Block
Ninewells Hospital
Dundee
DD1 9SY

Date: 29 January 2009
Your Ref:
Our Ref: FB/LR/08/S1401/133
Enquiries to: Miss Fiona Bain
Extension: Ninewells extension 32701
Direct Line: 01382 632701
Email: fionabain@nhs.net

Dear Ms Swanson

Full title of study: Neuropsychological Correlates of Anorexia Nervosa
REC reference number: 08/S1401/133

Thank you for your letter of 19 January 2009, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Sub-Committee.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

The favourable opinion applies to the research sites listed on the attached form.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission at NHS sites ("R&D approval") should be obtained from the relevant care organisation(s) in accordance with NHS research governance arrangements. Guidance on applying for NHS permission is available in the Integrated Research Application System or at <http://www.rdforum.nhs.uk>.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:



Document	Version	Date
Letter from College of Humanities and Social Science		14 November 2008
References for Literature cited in Application	1	13 November 2008
Letter from Stirling University		10 November 2008
Priory Insurance		01 July 2008
Letter from Priory		05 November 2008
Participant Consent Form	1	13 November 2008
Questionnaire: SPSI		
Questionnaire: SLCS		
Questionnaire: Y-BOCS		
Questionnaire: SCL-90		
Letter from Sponsor		11 November 2008
Covering Letter		17 November 2008
Protocol	3	14 November 2008
Investigator CV		13 November 2008
Application	1	17 November 2008
Flowchart of protocol in non-technical language	1	13 November 2008
Intyerview schedule - The Eating Disorder Examination (EDE)		
Summary CV for supervisor		13 November 2008
the University of Edinburgh - Professional Indemnity Insurance Renewal Date: 01/082009		05 September 2008
Response to Request for Further Information		19 January 2009
Participant Information Sheet: University of Stirling	2	19 January 2009
Participant Information Sheet: Tayside Eating Disorders Service	2	19 January 2009
Participant Information Sheet: Priory Hospital	2	19 January 2009

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Now that you have completed the application process please visit the National Research Ethics Website > After Review

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

The attached document "After ethical review –guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Progress and safety reports
- Notifying the end of the study



The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email referencegroup@nres.npsa.nhs.uk.

08/S1401/133

Please quote this number on all correspondence

Yours sincerely



Dr. Carlos Wigderowitz
Chair

Email: ethicshelpline.tayside@nhs.net

Enclosures: "After ethical review – guidance for researchers"
Site approval form

Copy to: Ms Elspeth Currie, Edinburgh Clinical Trials Unit
NHS Tayside R&D office



Appendix 10 Consent form



Consent Form

Title of Project: Neuropsychological Correlates of Eating Disorders in Adult Females

This form must be completed and signed by the subject in the presence of someone with knowledge of the research designated by the Principal Investigator. This may be a doctor, nurse, clinical psychologist or other member of the research team who must countersign the form as witness to the subject's signature.

1. I confirm that I have read and understood the subject information sheet for the above study.
2. I have had an opportunity to ask questions and further discuss the study; and have received satisfactory answers to all my questions. I feel I have now received enough information about the study.
3. I understand that my participation is entirely voluntary and that I have the right to withdraw from the study at any stage without giving a reason. I understand this will have no impact on my present or future medical care. If I decide to withdraw from the study the data already collected with consent will be retained and included in the study analysis.
4. I understand that all information collected during study participation will be confidential. Confidentiality may be limited if there is an issue of risk to myself or others, in which instance the Clinical/University staff will be informed.
5. I agree to participate in this study.

_____ Name of Subject	_____ Signature	_____ Date
_____ Name of Witness	_____ Signature	_____ Date

Appendix 11 Graphs of Correlations relating to Additional Results section

EDE Restraining and Phobia (SCL-90-R)

